# Studies in the history of ideas on the origin of life from 1860.

Kamminga, H

# STUDIES IN THE HISTORY OF IDEAS ON THE ORIGIN OF LIFE FROM 1860

A thesis presented by Harmke Kamminga for the degree of Doctor of Philosophy in the University of London.

Department of History and Philosophy of Science

Chelsea College

University of London

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HARMKE KAMMINGA

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## ABSTRACT

The aim of this thesis is to place the history of ideas on the origin of life in a wider theoretical framework. The problem of the origin of life came into focus in the 1860s, through a conjunction of Darwin's theory of evolution, which implied that all life on earth had ultimately descended from a simple primordial cell, and Pasteur's work on spontaneous generation, which suggested that even the simplest known organisms could not arise independently of any parent. The resulting dilemma led to the formulation of several hypotheses of the primordial origin of life on earth. It will be shown that these hypotheses were inspired primarily by their authors' views on the nature of life and remained without a sound scientific basis for many decades.

It is only in the last 30 years that investigations into the origin of life have developed into an active field of research and the factors responsible for this transition are analysed. In this context, a study is made of the theory of the Soviet biochemist Aleksandr Oparin, whose work was instrumental in opening up an experimental approach to the problem. Oparin's main innovation consisted in the fruitful use he made of developments in a wide range of scientific disciplines, especially in biochemistry. It is the rich chemical and biochemical content of Oparin's theory also that sets it apart from the main contemporary rival hypothesis, according to which life began with the formation of nucleic acids and a primitive genetic apparatus.

In an examination of the relevant scientific, methodological and philosophical issues, the heuristic value of a materialistic approach to the problem of the origin of life is acknowledged, but the differences in explanatory power between various hypotheses are attributed primarily to differences in their scientific content.

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# PREFACE

Questions of origin and development pose a serious challenge for the philosopher of science, namely the challenge to develop a methodology of the historical sciences that will be of heuristic value to the natural scientist. This daunting issue first stimulated my interest in the problem of the origin of life - a subject that had gained "scientific respectability" only in recent years, against a background of complex interactions between several scientific disciplines, methodological issues, and fundamental questions concerning the nature of life. Soon after I had begun to explore this rich source of philosophical questions, however, it became clear that what was needed first of all was a historical analysis of recent ideas on the origin of life. I am deeply grateful to Dr. Melvin Earles, my supervisor, for having encouraged me to direct my research along these lines and for his continual support and constructive criticism. I am also indebted to Chelsea College for the award of a College Studentship which enabled me to devote three years to full-time study in the Department of History and Philosophy of Science. I further wish to thank all members of staff and students of this Department for providing a stimulating and critical environment.

The progress on this thesis has been helped greatly by discussions with numerous historians and philosophers of science. I am particularly grateful to Nils Roll-Hansen in Oslo for his stimulating comments and for providing me with preprints and reprints of many valuable articles; to Dr. Aleksei Shamin of the Biochemical History Group in Moscow for interesting discussions and for sending me a complete bibliography of Professor Aleksandr Oparin; and to David Bearman, former Secretary of the Survey of Sources in the History of Biochemistry and Molecular Biology, for providing biographical information on several scientists currently active in the field of the origin of life. I am permanently indebted to Steve Prentis for his unwavering support and encouragement, for his comments on several drafts of every chapter of this thesis, and for giving me information on some of the recent developments in the field of the origin of life. Finally, I should like to thank Beryl Attwood for her rapid and flawless typing of this rather massive manuscript.

It was with deep regret that I heard of the death of Professor Oparin on April 21st this year. His work has inspired many of the ideas expressed here and I should have felt honoured if he could have read this thesis, as a small tribute to his profound contributions.

Harmke Kamminga

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## INTRODUCTION

The problem of the origin of life has received little attention from historians and philosophers of science. Yet this is an area where ideas on the nature of life, methodological issues concerning the investigation of vital phenomena and theoretical developments in the biological sciences have interacted in a particularly revealing manner. Moreover, while speculations on the origin of life were long held to be the prerogatives of theologians and metaphysicians, over the past 30 years investigations into the question have developed into an active field of scientific research. This raises the historical question of what factors were responsible for this transition. The primary aim of this thesis, therefore, will be to place the history of ideas on the origin of life in a wider theoretical context, paying attention to basic philosophical assumptions, to questions of scientific methodology and to advances in scientific knowledge*.

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*The few previous historical and philosophical accounts of the problem of the origin of life have tended to concentrate on just one or two of these three classes of factors. For example, Hilde Hein has discussed the question in the context of the debates between mechanism and vitalism and their implications for the methodology (and especially the heuristics) of the biological sciences without, however, considering the scientific background of the problem (1). Thomas Hall, in his _Ideas on Life and Matter_, has related the views on the origin of life of some biologists to their concepts of the nature of life (2). Within the vast scope of Hall's work, however, the question of the origin of life does not occupy a central position and it is not analysed in detail. In 1933, C.B.Lippmann presented an exhaustive catalogue of ideas on the origin of life from antiquity to the early 20th century (3). Lippmann's somewhat dismissive treatment is accompanied by little analysis and concludes with the observation that the subject belongs in the sphere of metaphysics rather than science. The approach adopted in this thesis also differs fundamentally from that of John Farley (4), as will be discussed below.

The thesis will be presented in two parts: Part I will discuss the historical background of the question of the origin of life from the early 1860s to approximately 1925, a period during which several approaches to the problem were formulated but little concrete progress was achieved; and Part II will deal with the central position taken by Aleksandr Oparin's theory of the origin of life in more recent studies of the subject.

In the 1860s, the problem of the origin of life on earth first became a subject of profound scientific interest. The reasons for this development must be sought in the convergence of three major scientific issues. First, the increasingly influential hypothesis of Kant and Laplace on the nebular origin of the solar system regarded the earth not as an unchanging object that had existed for eternity, but as a historical product of the evolution of matter. The hypothesis implied that the earth was once far too hot to sustain life and, therefore, that life on earth must have had a definite origin in time. Secondly, Darwin's theory of evolution demanded some starting point, some type of primordial cell from which all present forms of life had ultimately descended. Darwin did not attempt to explain in <u>The Origin of Species</u> how such primordial organisms had come into being on a once lifeless earth, but his work encouraged a search for an explanation of this question in natural, historical terms. Thirdly, Pasteur's experiments on spontaneous generation in the early 1860s showed that sterilised infusions of organic matter remain sterile providing that contamination with pre-existing organisms is prevented. In other words, Pasteur's work suggested, and to many proved, that living organisms do not arise spontaneously from non-living matter. In conjunction, these three points gave rise to the following problem: simple living organisms must have first appeared on earth in the absence of pre-existing organisms; but there was no evidence that life, even in its simplest known forms, could arise from non-living matter. How then could the first appearance of life on earth be accounted for in terms of natural causes?

One way out of the dilemma was simply to deny that Pasteur's results had refuted the doctrine of spontaneous generation and to continue producing what were thought to be counter-examples. The most tenacious advocate of this position was Henry Charlton Bastian, whose experiments on spontaneous generation continued well into the 20th century. His work will be discussed in Chapter I. Bastian's position, however, was an isolated one. A more common response to Pasteur's work was to accept its validity but to deny that it had any bearing on the origin of extremely simple organisms in the long-distant past. Many argued that under the special, if unknown, conditions of the primitive earth a gradual transformation of carbon compounds into very simple living systems must have taken place. This idea formed the basis of the hypothesis of evolutionary abiogenesis, upheld by many prominent biologists, such as Thomas Huxley, Ernst Haeckel, Carl Nägeli and Eduard Pflüger. Their hypotheses, which will be discussed in Chapter II, are the precursors of modern views on the question. In a related, but different category was the work of those who saw the natural transition from non-living into living matter primarily in terms of the action of some supposedly fundamental force, such as osmosis. Experiments carried out to demonstrate the essential nature of various natural forces for the generation of life will be described in Chapter V.

A third solution of the dilemma was to impose a rigid interpretation on Pasteur's results, to accept that life is necessarily antecedent to life and to deny that life in the universe had ever had an origin in time. The concept of the eternity of life was central to two different theories. One, the theory of panspermia, maintained that protoplasmic bodies had always existed on some planet and had populated other celestial bodies after travelling through space. The various hypotheses proposed to explain how living organisms were transferred from planet to planet will be discussed in Chapter III. According to the second theory in this category, life was not only eternal but actually prior to the inorganic world: it was life that had produced inorganic nature, just as protoplasmic organisms excreted inorganic products (see Chapter IV).

In the discussion of these hypotheses, assumptions regarding the nature of life and methodological issues will be analysed where relevant. In the final chapter of Part I a more thorough examination of the influence of materialist philosophies on 19th-century ideas on the origin of life will be made, with special reference to the work of Ernst Haeckel.

It should be pointed out that, with the exception of the work of Bastian, the question of the origin of life will be treated as distinct from the issue of spontaneous generation. In contrast, John Farley has argued that the two questions were inextricably interwoven during the period under discussion. This thesis is not written in reply to Farley's work, but in order to clarify the different approach adopted here, some comments on Farley's argument are warranted at this stage.

In his book on the spontaneous generation controversy (see ref. 4), Farley takes issue with the traditional account that the doctrine of spontaneous generation was undermined progressively by the experiments of Redi, Spallanzani, Pasteur and others. Backed by a wealth of historical material, Farley argues convincingly that the issue of spontaneous generation disappeared and reappeared with theoretical developments in biology, with the rise and fall of philosophical systems and with different interpretations of scripture. In the second half of the 17th century, for example, the possibility that organisms arise de novo was rejected on theoretical grounds as a consequence of the wide acceptance of William Harvey's ovist theory, according to which all living beings are derived from an egg cell, or ovum. Redi's experiments, which showed that maggots which appear in decaying meat are in fact the larvae of flies who lay their eggs on the meat, should be seen against this background (5). Later, in the mid-18th century, the popularity of epigenetic, as opposed to preformationist, theories of development lent support to the idea that organic matter has the potential of organising itself into individual living organisms. In fact, Spallanzani's attempts to refute spontaneous generation were inspired by his opposition to the theory of epigenesis (6). In the late 18th century, spontaneous generation became an integral part of both French materialism and of German Naturphilosophie (7). According to Farley, its association with atheism and the politics of the French Revolution in the former case and with vitalistic doctrines in the latter, subsequently made the concept of spontaneous generation highly suspect in France and Germany, respectively.

In the most controversial part of his book, Farley attempts to deflate the importance of Pasteur's contribution to the solution of the problem of spontaneous generation and credits Oparin with having finally settled the dispute in the 1930s by virtue of his theory of chemical evolution. Farley argues that the undeniable impact of Pasteur's work in France was largely due to a political and religious reaction against the materialistic ideas of the French revolution (8). He maintains that previous historical accounts have overestimated Pasteur's role as a result of a naive interpretation of the significance of the experimental method in the progress of biology. The two main arguments presented in support of this claim are the following: first, Pasteur's experiments were not "crucial experiments" because it is logically impossible for any finite series of experiments to establish that spontaneous generation can never occur under any circumstances. Secondly, it is a matter of historical fact that the controversy was not settled by Pasteur's work, as illustrated by subsequent debates concerning the possibility of abiogenesis, with special reference to the question of the origin of life on earth.

Farley's first argument will be examined further in Chapter I, where the methodological positions of Pasteur and Bastian will be compared. Suffice it to say here that Pasteur's experiments were not simply isolated demonstrations of the non-occurrence of spontaneous generation, but that they were conducted against the background of a rival theory: according to Pasteur, previous claims that spontaneous generation had been demonstrated were to be explained in terms of contamination with pre-existing organisms present in the environment. His own negative results could be accounted for by the fact that he had taken careful precautions to prevent such contamination. Hence, Pasteur provided a rational, if not logically conclusive, alternative to the idea that organisms can arise suddenly from non-living matter. It is important to realise, however, that Pasteur's theory of contamination did not, and was not intended to, explain the origin of life on a once lifeless earth*. Hence, the problem of spontaneous generation as an every-day occurrence and the question of the origin of life on earth became clearly demarcated for the first time. In addition, those who considered Pasteur's results to be generally applicable were left without an explanation of the generation of life from non-living

*The theory of panspermia, based on the idea of a cosmic presence of space-travelling germs (see Chapter III), could be seen as an attempt to account for both problems by means of the same theory.

matter. This state of affairs led to a crisis in the field of the origin of life, as illustrated by the many rival hypotheses that were proposed in the ensuing decades, by the bizarre nature of some of these hypotheses, and by the fact that they all speculated far beyond contemporary scientific knowledge.

By Farley's second argument, the approach of the evolutionary abiogenesists to the problem of the origin of life is placed in the same category as a belief in spontaneous generation, which Farley defines as the belief that "some living entities may arise suddenly by chance from matter independently of any parent" (9). However, the evolutionary abiogenesists are to be distinguished from the adherents of the doctrine of spontaneous generation on several accounts. First, they did not oppose Pasteur but, on the contrary, accepted that life does not now arise <u>de novo</u> and certainly not suddenly. In general, they relegated the process of abiogenesis to the long-distant past and relied on some crucial, but unknown, change in environmental conditions to account for the fact that the process is no longer observed to be at work in nature. Secondly, they did not view the origin of life as a sudden chance event, but as a gradual process determined by the inherent properties of carbon compounds and by the special conditions of the prebiotic earth. The slow and gradual nature of the process came to be emphasised more and more as the complexity of even the simplest known organisms became evident. These points will be discussed in greater detail in Chapter II, where it will also be shown that explicit, if imperfect, hypotheses of a gradual chemical evolution preceding the origin of life were proposed as early as in 1875.

One further point needs to be made in this context. The theoretical confusion in the field of the origin of life in the 19th century was reflected in the introduction of many different terms to denote the transition from non-living to living matter, such as Huxley's abiogenesis, Haeckel's autogony and archigony, and Bastian's archebiosis. The general term used most often in the German literature was Urzeugung, which literally means "primordial generation" (from Ur-, primitive, original, primordial; and zeugen, procreate, generate, produce). The standard dictionary translation of this term is given as spontaneous generation or abiogenesis and in 19th-century translations from German into English, Urzeugung was frequently translated as spontaneous generation, even when it is clear from the context that a gradual process was envisaged instead of a sudden transition*. The term must therefore be interpreted according to the context in which it was used and, on the whole, may best be left untranslated. Abiogenesis may often seem to be a direct equivalent, but here again care must be taken. Huxley introduced the term abiogenesis to denote the generation of life

*For example, E.R. Lankester translated Nägeli's phrase "Die Urzeugung leugnen heisst das Wunder verkunden" (10) as "To deny spontaneous generation is to declare miracles" (11). Nägeli, however, postulated three stages in the generation of life from non-living matter: a prolonged accumulation of organic matter resulting in the formation of protein; the organisation of protein matter into a micellar network; and the individualisation of this micellar mass into primitive living organisms, or probionts. Incidentally, Lankester himself pointed out the differences between this type of approach and traditional views of spontaneous generation (12).

from non-living matter and it came to be used subsequently to describe the generation of life directly from inorganic matter. In the 19th-century literature, however, the term inorganic was often used in the biological (meaning non-living) instead of the chemical sense. Huxley himself, when speculating on the origin of life from inorganic matter, included organic molecules such as oxalates and tartrates among the materials present in the environment in which life arose in the long-distant past (13). It must be remembered, then, that statements regarding the origin of life from inorganic matter did not automatically exclude a development of organic matter (in the chemical sense) prior to the transition to life. Such a development was implicit in some of the earlier writings on the subject and explicit in most writings from about 1875 onwards.

In view of the above remarks, Farley's presentation of the 19th-century debates concerning the origin of life from non-living matter as simply another aspect of the controversy surrounding spontaneous generation seems misleading. Historically, and by Farley's own definition, spontaneous generation referred to the appearance _de novo_ of organisms over a matter of hours, days, weeks or, at the most, a few months. This traditional concept of spontaneous generation was theoretically redundant to those who adopted an evolutionary approach to the origin of life*, an approach that was clearly more refined.

*This point is highlighted by Farley himself when he writes: "It is difficult to understand why Tyndall was so opposed to the doctrine of spontaneous generation, given his being both a materialist and an evolutionist" (14). Tyndall's position (see Chapter II), and that of many others (cont. next page)

It is suggested, therefore, that the question of spontaneous generation in the sense of the sudden appearance de novo of fully formed organisms was settled to all intents and purposes by Pasteur and his supporters, while the problem of the origin of life was brought into sharp focus at the same time.

What the evolutionary abiogenesists of the 19th century provided was an approach to the question of the origin of life and not any theory with a solid scientific basis. It is in this latter respect that Oparin provided a fresh impetus to the field and his work far transcends any contribution he may have made towards finally laying to rest the ghost of spontaneous generation. Part II of this thesis will examine the content, the scientific basis and the impact of the theory Oparin presented in 1936 (15). At a time when the problem of the origin of life had reached a clear impasse, he proposed a detailed theory of the stages involved in the processes that might have led to the primaeval development of life on earth. As will be shown in Chapter VII, earlier notions of chemical evolution were given substance by Oparin's attempt to define the specific conditions under which organic compounds necessary for life could have been formed abiogenically. Drawing on inorganic, organic and colloid chemistry, biochemistry, geology and astrophysics, Oparin was able to trace the possible development of primitive organisms and the early evolutionary stages

(footnote cont.) who adopted a similar stand, is not difficult to understand once one accepts the distinction between the concept of spontaneous generation in its traditional sense and the evolutionary abiogenesist hypothesis of the origin of life.

of life on earth. Astrophysics and geology provided Oparin with the data he needed to formulate a picture of the conditions on the prebiotic earth. Chemistry told him how organic matter could have been formed and how it had become progressively more complex under these conditions. Work in colloid chemistry provided the inspiration for Oparin's coacervate hypothesis, which accounted for the initial separation of prevital organic bodies from the general environment. Finally, biochemical and microbiological research into metabolism provided Oparin with the information upon which he built his hypothesis of the evolutionary sequence of early life on earth. As will be shown in Chapter VIII, Oparin's theory of the early development of life on earth reflects the preoccupation of biochemistry in the first three decades of the century with metabolic processes and enzymatic reactions.

While Oparin provided scientists interested in the origin of life with a fruitful research programme, there was a significant omission in his theory. In 1936, Oparin made no attempt to describe any possible pathways by which biological mechanisms of replication might have evolved. To Oparin, metabolism was the fundamental feature of life and it was in terms of metabolism that the transition from prevital systems to primitive living organisms was to be explained. In contrast, the main contemporary and current rival hypothesis holds that life began with the formation of the hereditary material and a primitive genetic apparatus. The historical and theoretical background of this genetic approach to the problem of the origin of life will be discussed in Chapter IX and the methodological basis of the conflict between the metabolic and the genetic schools will be examined in Chapter X. In this context, some comments must again be made on Farley's treatment of this issue.

Farley attributes Oparin's success in formulating a rational theory of the origin of life primarily to the dialectical materialist approach he adopted (16). This argument is incomplete, however, as it ignores the scientific context in which Oparin's theory developed. The relations between dialectical materialism and natural science are by no means straightforward and the dialectical method cannot be understood clearly in isolation from the empirical background within which it is applied. Dialectical materialism stresses the importance of historical processes and of questions of origin and development. In this sense, it was of great heuristic value and encouraged Oparin to take the question of the origin of life seriously. In addition, however, Oparin's work should be seen against the background of the scientific, and especially the biochemical, developments that will be examined in Chapter VIII. It is the rich chemical and biochemical content of Oparin's theory that sets it apart most strikingly from the hypotheses of his predecessors. Moreover, the primary distinguishing feature between Oparin's theory and the genetic rival hypotheses is also one of scientific content. Farley presents the debate between the metabolic and genetic schools of thought on the origin of life as a conflict between dialectical materialism and reductionism. Again, however, the antithesis is not clear-cut. The method of reducing all vital phenomena to the properties of the genetic material is indeed inconsistent with a dialectical approach, but it is also inconsistent with a biochemical approach which stresses the complex interactions between molecules and supramolecular structures within living systems. These issues will be discussed in Chapter X in the context of the different theoretical backgrounds of the two approaches.

Besides providing a theory with a sound scientific basis, Oparin's work also opened up an experimental approach to the problem of the origin of life, starting in the 1950s with the abiogenic synthesis under putative prebiotic conditions of numerous molecules that play a role in living organisms. This experimental phase will be discussed in the final chapter as a further illustration of the heuristic value of Oparin's work. A number of fundamental questions concerning the origin and early development of life remain to be solved and these will also be examined in Chapter XI.

As has been stated before, the aim of this thesis is to place the history of ideas on the origin of life in its wider scientific, methodological and philosophical context. No attempt will be made to analyse in detail the social and political factors that may have influenced progress in the field. It will be taken for granted, for example, that Oparin's interest in dialectical materialism was stimulated by the intellectual climate of the socio-political environment of post-revolutionary Russia. It is not denied that such external questions are of interest, but any investigation of these questions should be based on a clear understanding of the scientific and methodological foundations of the history of the problem. It is hoped that this thesis will contribute towards the attainment of this understanding.

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# PART I

## HISTORICAL BACKGROUND, 1860-1925

## Chapter I
## THE DYING EMBERS OF SPONTANEOUS GENERATION: BASTIAN'S THEORY OF ARCHEBIOSIS

In Lamarck's theory of evolution, organisms that arose spontaneously by the action of physical forces formed the starting point for biological evolution (1). By the time Darwin's The Origin of Species was published, however, much doubt had been thrown on the concept of spontaneous generation (2) and Darwin himself refrained from speculating on the mode of origin of a primordial form of life on a once lifeless earth. The problem of the origin of life, independent of pre-existing organisms, became particularly acute when Louis Pasteur (1822-1895) appeared to have settled the question of spontaneous generation once and for all.

In 1859, Felix Pouchet (1800-1872) published a work in which he reported demonstrations of the spontaneous generation of living organisms, Hétérogenie ou traité de la génération spontaneé (Heterogenesis or treatise on spontaneous generation). The French Academy of Science was sceptical of Pouchet's work and announced that the Prix Alhumbert for 1862 was to be awarded to the scientist who could throw new light on the question of spontaneous generation by means of well-conducted experiments (3). The prize was awarded to Pasteur for a series of experiments carried out in 1860 and 1861. Briefly, his major results were the following. First, Pasteur showed that microscopic examination of dust in the air, collected by drawing air through a cotton plug by suction, revealed the presence of large numbers of particles that were indistinguishable from germs and spores (4).

Secondly, he showed that boiled infusions in swan-necked flasks (the necks being drawn out and curved in a variety of ways) remained free of microorganisms even when open to the air, presumably because germs in the air settled in the curvature before reaching the interior of the flasks (5). Thirdly, he showed that exposing sterile infusions to the air in different environments resulted in varying degrees of subsequent microbial growth: more flasks showed growth in his laboratory than in the still air of the vaults of the Paris Observatory. Moreover, at the foot of the Jura plateau, eight out of twenty flasks produced bacterial growth; in the Jura mountains, at an altitude of 850 metres, five out of twenty flasks exhibited growth of organisms, as compared with only one out of twenty at a height of 2000 metres, where Pasteur expected very few germs to be present in the air (6). Pasteur's experiments suggested that organisms do not appear in sterilised infusions if contamination with pre-existing organisms is prevented and that the concept of spontaneous generation should be abandoned.

Although the impact of Pasteur'swork was profound, this conclusion was not accepted universally. Pouchet and his co-workers did not accept it, for example, but the most tenacious opponent of Pasteur was Henry Charlton Bastian (1837-1915). Bastian was Professor of Pathological Anatomy at University College, London, and Physician at University College Hospital (7). He was a recognised authority in the field of neurology but is chiefly remembered for his stand on spontaneous generation. A typical assessment of Bastian's contributions is given by

Lechevalier and Solotorovsky:

> "The last important heterogenesist was Bastian. In 1872 he published a huge book entitled The Beginnings of Life in which he stated his belief in spontaneous generation. With unusual determination he held to his faith in spite of the fact that his arguments were destroyed with monotonous regularity by Pasteur and his collaborators. It was through the objections of Bastian, however, that more was learned about the effect of acidity on the survival of bacteria exposed to heat." (8)

Similar, but slightly more extensive, treatments are to be found in the histories of Bulloch (9) and Oparin (10). In contrast, John Farley presents Bastian as a victim of the arrogance of Pasteur and his supporters and credits Bastian with having a better grasp of the scientific method than his contemporaries who opposed spontaneous generation (11). Before discussing Bastian's ideas on the origin of life from lifeless matter, it is therefore of interest to examine first his position on the issue of spontaneous generation in general.

Bastian's work on spontaneous generation

Bastian's publications on spontaneous generation span two periods, from 1870 to 1877, after which he remained silent on the issue for many years, and from 1903 to 1911. The experiments he performed during the first period presented a serious challenge to the widely held view that all life is destroyed by boiling for 5-10 minutes. Bastian himself never wavered from the conviction that the limit of vital endurance in liquid media is 100°C, although he pointed out that the thermal death point of some organisms might be as high as 130°C *in vacuo* or in dry air (12). Any growth of organisms in infusions that had previously been boiled was, therefore, interpreted by him as a demonstration of spontaneous generation. In the 1870s, he reported a vast number of such demonstrations and presented his arguments in favour of the concept of spontaneous generation in a series of long papers and several books.

In 1871, Bastian published a brief monograph entitled The Modes of Origin of Lowest Organisms (13), a highly polemical work which set out the main points that recurred in all his subsequent writings on the subject. First of all, he rejected the claim that all life must come from life because it was, in his view, clearly contradicted by experience. He then considered four different ways in which bacteria could come into being: direct homogenesis, indirect homogenesis, heterogenesis and archebiosis. Direct homogenesis was the reproductive method whereby bacteria are derived from pre-existing bacteria of the same kind by fission. Indirect homogenesis referred to a process whereby bacteria were allegedly derived from more complex organisms, such as fungi, into which they developed again later. In this case, bacteria represented subordinate stages in the life history of, for example, the fungus. Bastian claimed that he himself had seen bacteria develop into mycelial structures resembling fungi*. Spontaneous generation of bacteria could take two forms: heterogenesis, which involved the reorganisation of minutes particles of living matter derived from other organisms; and archebiosis, a process which gave rise to bacteria independently of pre-

*It is likely that the development observed by Bastian involved fungal spores rather than bacteria. Alternatively, he may have observed the differentiation of the amoebae that represent a stage in the development of cellular slime moulds.

existing living things.

Bastian drew support for heterogenesis from his observations that bacteria are found in vegetable cells, even from the central parts of plants, when these are sickly or dying, and also in epithelial cells taken from the mouth. According to Bastian, the number of bacteria found in such cells was directly proportional to the malnutrition or lack of vitality of the individuals from which the cells were taken. He suggested that when the vital activity of an organism is on the wane, its constituent particles "individualise" themselves and grow into other organisms such as bacteria. The alternative hypothesis would, according to Bastian, have to assume that microorganisms are universally distributed through the tissues of higher organisms. This Bastian could not accept:

> "To suppose that actual germs of bacteria and of torulae* are uniformly distributed throughout the tissues of higher organisms, is to harbour a hypothesis which would appear to many to be devoid of all probability - more especially when the heterogenic origin of larger and higher organisms is a matter of absolute certainty." (14)

Bastian's arguments in favour of archebiosis** were based on the invariable association of microorganisms with fermentation processes. He took issue with the conclusion of Pasteur and others that fermentation is actually caused by these organisms:

> "They think that those organisms which serve to initiate the changes in question [i.e. fermentations], have been derived from a multitudinous army of omnipresent atmospheric germs, which are always ready, in number and kind suitable for every emergency." (15)

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*In Bastian's writings, the term torulae referred to fungal and yeast cells.

**At this stage, Bastian only considered archebiosis of organisms in fluids containing organic matter devoid of life. He later extended his claims to inorganic starting compounds (see below).

But Bastian denied that Pasteur had demonstrated the presence of bacteria in the air: Pasteur had merely shown the presence of corpuscles that showed some external resemblance to infusoria, the spores of fungi, etc. For this reason, Bastian favoured Liebig's interpretation that fermentation is a purely chemical process, in which living organisms play no causative role, and concluded that, on the contrary, the action of chemical ferments produces the organisms*.

Bastian's small monograph was soon followed by a much more extensive treatment of heterogenesis and archebiosis, in The Beginnings of Life (16). This work, published in 1872, was published in two volumes comprising a total of more than 1200 pages. In these volumes, Bastian expounded his views on the nature and origin of life in great detail and described a large number of experiments in support of his theories. The main themes are introduced in the Preface: Bastian here stated that all bacteria are killed when exposed to a temperature of 140°F and yet his own experiments had shown that organisms will appear in sealed flasks preheated to temperatures of up to 300°F. According to Bastian, these organisms must therefore have arisen de novo and spontaneous generation was an established fact. He then presented a materialistic interpretation of spontaneous generation and argued that such a view was indispensable both for the explanation of the origin of life on earth and for the explanation of the persistence of lower organisms, such as

*By this time, Bastian's position on fermentation was a minority one. The issue of fermentation, and especially Pasteur's contributions in this area, will be reviewed in Chapter VIII of this thesis.

bacteria and amoebae, throughout the course of evolution. It was believed by many that the molecular properties of carbon compounds could lead to the formation of ever more complex combinations and that such processes had generated life on the primaeval earth. Bastian added:

> "And if such synthetic processes took place then, why should they not take place now? Why should the inherent molecular properties of various kinds of matter have undergone so much alteration?" (17)

With respect to the abundance of very simple forms of life, Bastian remarked that it was incredible that, say, amoebae should have existed for millions of years without undergoing any differentation:

> "Would the evolutionist have us believe that the simplest and most structureless Amoebae of the present day can boast of a line of ancestors stretching back to such far-remote periods that in comparison with them the primaeval men were but as things of yesterday? The notion surely is preposterously absurd; or, if true, the fact would be sufficient to overthrow the very first principles of their own Evolution philosophy." (18)*

Bastian felt that it was much simpler to assume that the lower forms of life are being generated continuously from non-living matter.

Throughout The Beginnings of Life Bastian emphasised that the

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*It would be anachronistic to accuse Bastian of ignoring the possibility that considerable evolution at the biochemical, rather than the morphological, level might have occured in the history of the lower organisms. On the other hand, Bastian appears to have had a somewhat Lamarckian view of evolution, implying that organisms were somehow compelled to evolve into higher forms of life. On a Darwinian view, any variation among a living group that was well-adapted to its habitat would have tended to the elimination of the new varieties (because they were likely to be less well adapted) and to the preservation of the original forms. Of course, other members of the species might well have evolved into "higher" species, resulting in divergence.

properties of life are the direct outcome of the properties of matter. The manifestations of life could not be independent of physical and chemical laws and both the substance and the vital phenomena of organisms were ultimately derived from the mineral world (19). Bastian pointed out that this view was now widely accepted and quoted from the works of authors having analogous opinions, for example Herbert Spencer and Thomas Huxley*. At the same time, he admitted that the concept of spontaneous generation had traditionally been associated mostly with vitalism (20). Earlier adherents of the doctrine, such as John Turberville Needham, Buffon and Pouchet believed only in heterogenesis, not in archebiosis (the generation of life in solutions that only contained mineral ingredients). Moreover, these investigators believed that heterogenesis was mediated by some special force, such as Needham's "force végétative", Buffon's vital "molecules organiques" and Pouchet's "force vital". In other words, the theories of these men were framed such as to exclude the possibility of their even contemplating the origin of living things from non-living matter. In the second volume of his work, Bastian phrased this point more strongly and stated that a denial of the possibility of archebiosis amounted to vitalism. According to Bastian, it was necessary to accept that

> "... there is a natural tendency amongst certain kinds of molecules to fall into combinations and rearrangements which terminate in the formation of 'living' matter." (21)

In Bastian's opinion, not only the formation of living matter,

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*For Spencer's and Huxley's views, see Chapter II of this thesis.

but also the generation of the characteristic shapes of organisms was guided solely by universal physical and chemical laws (22). He argued that the causes that determine the form and structure of crystals were similar in kind to the causes determining organismic form. Even the simple precipitation of lime carbonate in a viscid solution of, for example, gum resulted in the formation of globules that showed a close resemblance in form to living cells. As the shapes of these globules were undoubtedly determined by the mere physical properties of their constituent molecules, Bastian concluded that the shapes of organisms (which were composed of complex "colloidal molecules") were also derived from the properties of their molecular components, as operated on by external conditions (23). Later he stated:

> "It seems, again, no more wonderful that the organism which develops de novo today should resemble another which develops from the spore of a pre-existing organism, than that a crystal which forms to-day in a saline solution should resemble another which is capable of arising by the growth of a portion detached from a similar pre-existing crystal. In all these cases, there is a similarity of product, because the crystalline or organic form produced is to be regarded as the physical expression of the harmonious actions which have led to their production - because the forms are the results of a physical necessity, and not of a mere blind chance." (24)

The Beginnings of Life also contains numerous attacks on Pasteur. According to Bastian, the untenability of Pasteur's conclusions arose from the fact that his experiments only gave negative results and Pasteur's attempt to draw definite conclusions from negative evidence was a reflection of his "defective reasoning" (25). Bastian again took issue with

Pasteur's views on fermentation and reiterated his contention that chemical fermentation resulted in the generation of living organisms (26). Pasteur's assumption that invisible and unknown germs exist in the air was unacceptable. The results of Bastian's own experiments showed that such germs, if they existed, would have to be capable of resisting a temperature far higher than that believed to be fatal to other, visible germs; this state of affairs would violate the "unity of natural laws". The alternative hypothesis of archebiosis, on the other hand, required no unwarranted assumptions. Finally, Bastian criticised Pasteur's support for the germ theory of disease: the origin of bacteria in the blood or in epithelial cells was due to heterogenesis, and not the result of infection (27).

The majority of the experiments described in The Beginnings of Life involved heating infusions of hay, turnip or cheese in sealed flasks to a temperature of 212°F (100°C) (28). Bastian claimed that, without fail, masses of microorganisms grew in the sealed flasks, and as all pre-existing organisms must have been killed by the heat, those growing subsequently in the flasks could only have arisen *de novo*. Although some of Bastian's observations were later confirmed by other investigators, few were willing to place the same interpretation on the results. Usually it was argued that Bastian's infusions should have been boiled longer or at a higher temperature in order to prevent the survival of pre-existing germs. In the absence of independent evidence, both arguments were of course circular. Bastian assumed that boiling killed all life and any organisms growing in boiled infusions in sealed flasks must therefore have arisen spontaneously. His opponents assumed that organisms could not arise de novo and therefore Bastian's methods of sterilisation must have been inadequate. Independent support for the latter view was subsequently obtained, through the work of John Tyndall (1820-1893) in England and Ferdinand Cohn (1828-1898) in Germany.

Tyndall became interested in the question of spontaneous generation during his investigations of the effects of light rays on gaseous matter. Using beams of light he revealed the presence of floating matter in the air and found that much of this suspended matter was destroyed by heat (29). He also reported that air collected in flasks in a cellar where the air was still and any dust had settled revealed no such suspended matter. Tyndall pointed out that these observations might be relevant to Pasteur's demonstration of the variable growth of microbes in flasks exposed to the air in different locations. When Tyndall entered the field of spontaneous generation, he was rebuked by Bastian in a letter to the editor of The Times. Bastian maintained that the issue of spontaneous generation pertained the biologist and the physician, not the physicist, and warned Tyndall that much irreparable damage could be done by his "amazing" methods of reasoning (30). Tyndall, however, continued to work on the problem and his investigations into the heat resistance of bacteria were particularly fruitful. Using infusions of fresh hay and turnip, Tyndall found that these were sterilised by boiling for only five minutes. When he used an infusion of old, rotten hay, however, even four hours of boiling failed to achieve sterilisation. In view of such variable results, Tyndall postulated that bacteria have different life phases, a thermolabile phase during which the organisms are killed rapidly upon boiling, and a thermostable phase during which the organisms are remarkably resistant to heat (31).

In the meantime, Ferdinand Cohn had made a systematic study of the properties of bacteria. During the course of these investigations, he discovered that the hay bacillus (Bacillus subtilis) often contained roundish refractive particles, or spores (32). He subsequently described the germination and development of the endospore of B. subtilis and provided evidence for its high resistance to heat (33). He also showed that the difficulty in sterilising Bastian's turnip and cheese infusions was due to the presence of sporing bacilli in the cheese.

As an outcome of this work, Tyndall devised the method of fractional sterilisation by discontinuous heating, the process that is now called Tyndallisation (34). By interrupting the boiling of infusions briefly, any bacterial spores are given the opportunity to germinate; renewed boiling, however, destroys the newly germinated bacteria before they develop spores. By repeating this process several times all spores and bacteria are eventually eliminated and no new organisms appear in infusions that have been subjected to Tyndallisation. In other words, specific conditions for the repeatable destruction of bacteria and their spores and for the prevention of subsequent bacterial growth had now been defined.

The methodologies of Pasteur and Bastian

As was pointed out in the Introduction of this thesis, Farley has argued that Pasteur's experiments did not settle the question of spontaneous generation. One of Farley's main arguments is based on the claim that there is a logical asymmetry between the positions of those who deny the possibility of spontaneous generation and those who assert its reality: while opponents of spontaneous generation can only have their theories refuted (by even a single demonstration of spontaneous generation) but not verified, the adherents of spontaneous generation can only see their theories verified but not refuted (35). Roll-Hansen has characterised this argument as an example of "naive falsificationism" (36). The strong refuting role attributed to experiment by philosophers such as Karl Popper has in fact come under severe criticism, notably from Imre Lakatos (37). According to Lakatos, no scientific theory is consistent with every single fact in its domain and a strict adherence to a falsificationist programme would leave the scientist without any theory whatsoever. In practice, scientists do not accept or reject a particular theory on the basis of experiment, but compare one research programme with another for its empirical, explanatory and heuristic content. As a result, theories are rarely deemed refuted before a new and better alternative is available. The final choice between alternative theories may be made in several ways: an experiment may be designed to decide between two rival theories; instead, the relevance of previous anomalies may only become clear in the light of a new theory and may be given the title of crucial experiment in retrospect; finally, the old theory may simply be abandoned without refutation by experiment. To give just one example, the one-gene/one-enzyme hypothesis was not refuted by experiment but simply replaced by a theory that asserted a one-to-one correspondence between genes (DNA sequences) and proteins in general*. On a Lakatosian view, then, the role of experiment in the historical succession of scientific theories is de-emphasised and wider theoretical issues come to play a predominant role.

Farley's criticism of the traditional view that the belief in spontaneous generation was overthrown by experimental proof is a pertinent one. In his discussion of the debates between Pasteur and his opponents, however, Farley gives insufficient consideration to the internal theoretical aspects of these debates**. The central issue is whether Pasteur provided an alternative theory to the doctrine of spontaneous generation and, if so, how his theory compared with that of his opponents. In fact, Pasteur did not simply maintain that spontaneous generation was impossible, but held that previous demonstrations of spontaneous generation were to be explained in terms of contamination with pre-existing germs present in the environment. Already in the 17th century, Antony van Leeuwenhoek had demonstrated the presence of large numbers of "animalcules" in rain

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*More recently, matters have become much more complicated with the discovery of discontinuous genes with intervening sequences and "intron-exon" relationships in eukaryotic cells (38).

**The same point is made by Roll-Hansen in his review of Farley's book (see ref.36) water, well water, river water, sea water, the human mouth, human excreta, etc. (39). Moreover, Pasteur himself had been confronted with the problem of contamination in his research into the reasons for repeated industrial failures in the fermentation of beet sugar into alcohol*. In his work on spontaneous generation, therefore, he set out to demonstrate the presence of germs in the air and to show that sterilised infusions would not produce any bacterial growth if proper care was taken to prevent contamination with germs in the air. His results bore out both claims. In addition, within the framework of his theory of the ubiquitous presence of germs, Pasteur could explain not only his own results but also those of his opponents. The latter, in contrast, failed to present a rational explanation of Pasteur's results. This is where the fundamental asymmetry between the two positions is to be found, a point that was recognised clearly by Thomas Huxley (1825-1895). In his address Biogenesis and Abiogenesis, delivered to the British Association in 1870, he challenged the supporters of spontaneous generation to explain how food was preserved effectively in air-tight containers if it was not for the exclusion of pre-existing germs (41). In response **, Bastian investigated a number of tins containing

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*In 1857, Pasteur showed that the fermentation vats contained not only an alcohol-producing yeast, but also a "yeast" which produced lactic acid (40). This study formed the starting point for Pasteur's work on fermentation, which will be discussed in Chapter VIII, but were clearly also of great relevance to his work on spontaneous generation.

**Many years later, Bastian wrote that Huxley had strongly supported Pasteur "though not having worked at the problem himself", thus hinting at Huxley's incompetence to speak of the matter at all (42).

soup and salmon and reported the following observations: first, food in tins did not invariably remain well preserved and he did not believe that such failures could always be explained in terms of errors in the canning process, such as inadequate sealing. Secondly, he observed the growth of bacteria and fungal filaments even in some canned foods that appeared to be well preserved by other criteria (43). Huxley, rightly, was not satisfied with this reply (44). Bastian had failed to define the conditions under which spontaneous generation could and could not occur; he never recognised the need for such a systematic investigation and stated simply that

> "Negative results in these experiments can of course prove little or nothing ..." (45)

Bastian saw no need to explain why he sometimes obtained negative results and continued to report large numbers of observations of microbial growth in boiled infusions. The empirical evidence was all-important*: he had seen with his own eyes that microorganisms arise <u>de novo</u> - just as it had been "seen" before that crocodiles are generated from the mud of the Nile and maggots from decaying meat. Should Pasteur have backed down in the face of such evidence, or were there independent criteria for preferring his own theory? The results of Pasteur's elegant experiments had confirmed the predictions he

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*Roll-Hansen has shown that Pouchet also placed excessive emphasis on empirical investigation, to the exclusion of any underlying theory (46). In addition, Pouchet rejected Pasteur's theory of contamination on the curious grounds that, on such a theory, each single germ growing in his infusions should have been derived from the small portion of air to which the infusions had been exposed; the air would have to be thick with germs (47). Pouchet consistently ignored the rapid multiplication of bacteria in suitable media.

made on the basis of his theory of contamination. The explanatory power of this theory was greater than that of his opponents in so far as it could explain both negative and positive results in a systematic manner. Moreover, Pasteur's theory had a positive heuristic, as illustrated by his later work on the "diseases" of wine, beer and the silk worm, his studies of fermentation and especially his work on infectious diseases in man and animals. If there was any fanaticism in Pasteur's opposition to the concept of spontaneous generation, it was probably based on his faith in this highly practical and fruitful research programme, instead of being grounded in the political and religious motives attributed to him by Farley.

This does not mean that Bastian's work could simply have been ignored. The growth of microbes in infusions of hay and of turnip and cheese after prolonged boiling did present counter-examples to the claim that no organisms would grow in boiled infusions sealed off from the air. But such a general claim was not in fact made by Pasteur, who already in 1860 reported that the lactic acid ferment in milk is not destroyed by heating at 100°C, but is killed when boiled under pressure at 110-120°C (48). It was Bastian who raised the statement that boiling kills all life to the status of a natural law, while Pasteur was open to the possibility that there were variations in the thermal resistance among different species of microorganisms and took the trouble to investigate at what temperature some species of bacteria are destroyed. With the discovery of bacterial spores, a definite explanation of the heat resistance of the hay bacillus and the cheese bacillus became available and precise conditions for their destruction could be devised. By this time, the position of Pasteur and his supporters was very strong indeed and even Bastian remained silent on the issue of spontaneous generation after 1877. It transpired later, however, that Bastian did not feel defeated.

Bastian's work on the origin of life

Bastian re-entered the field of spontaneous generation in 1903, with the publication of Studies in Heterogenesis (49). In this large work, he presented a mass of strange results, showing the transformation of the matter of one organism into organisms of a totally different species, such as the transformation of Euglenae and plant cells into amoebae. In the Foreword of a later work, Bastian explained that he had stopped publishing on the subject because all his energy had been needed in other directions. He wrote:

> "I was, in fact, supposed to have been beaten out of the field, and my silence during these years perhaps lent some support to the notion." (50)

In 1898, however, he resigned from his posts at University College in order to start fresh investigations on the problems of heterogenesis and archebiosis. This section will concentrate on Bastian's work on archebiosis and the conclusions he drew from this work with respect to the origin of life from lifeless matter.

Bastian's views on the abiogenic origin of life had first been discussed in detail in 1872, in The Beginnings of Life (51). Here he had pointed out that his materialistic interpretation of archebiosis was consistent with the evolutionist hypothesis of the origin of life, according to which a gradual formation of organic matter on the primaevel earth had preceded the appearance of living things*. Bastian differed from the evolutionists, however, in that he believed that the generation of living forms from non-living matter was an every-day process that had occurred ever since the appearance of the first living forms. He saw no reason to postulate that archebiosis could only occur under special, unknown conditions that were prevalent only on the primitive earth and maintained that such a view would violate the principle of the uniformity of natural processes**. As has been mentioned above, Bastian also felt that his theory had the advantage that it could explain the persistence of lower organisms throughout the course of evolution.

These points were again raised in The Origin of Life, published in 1911. After a brief discussion of the evolutionist hypothesis of the origin of life, Bastian announced that he intended to settle the question whether archebiosis occurred only once or whether it was still taking place. On the basis of his principle of the "Uniformity of Natural Phenomena", he believed that life-evolving processes had continued ever since archebiosis had started and stressed the

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*See Chapter II of this thesis.

**It will be argued in Chapter II of this thesis that one of the principal weaknesses of 19th-century evolutionist hypotheses on the origin of life was their failure to define the special conditions of the primitive earth.

> "...strong probability that the physicochemical processes which originally led to the birth of living matter would similarly and constantly tend to be reproduced." (52)

The question had to be settled by proper experiments, however, and these he had now performed. Instead of using organic infusions, he had relied on solutions

> "...such as alone would have existed on the surface of the Earth when life-evolving processes were first initiated." (53)

His results were of "such a decisive nature" that he believed he had finally solved the problem of the origin of life (54) and submitted the results to the Royal Society. The paper, however, was refused, without an explanation being given "as usual" and Bastian thereupon decided to present his results in a book.

In the introductory chapter of the book, Bastian emphasised that many others had pointed out the irrelevance of Pasteur's results to the question of the origin of life under conditions other than those of the experiments. On the other hand, many authors who expressed this view had made discouraging remarks about the difficulties of reproducing the conditions under which life arose in the past and about the uselessness of attempting to produce protein as long as its complex structure was unknown. Bastian disagreed: the actual steps of the process were outside the range of biological enquiry and the problems connected with building up complex organic compounds were to be left to the chemist and the physicist. The biologist might legitimately enquire whether solutions could be devised which would, "as a result of natural tendencies", lead to the appearance of living units after exposure to particular conditions (55). This is what his experiments were designed to do.

The remainder of the book is taken up with the presentation and discussion of Bastian's results. After experimenting with solutions containing various ingredients that could be assumed to have been abundant on the lifeless earth, Bastian settled for two different solutions: one was yellow and contained, to each ounce of distilled water,

> "...only a few drops of a dilute solution of sodium silicate, together with about three times as many drops of liquor ferri perinitratis,..." (56)

The other solution was colourless and, to each ounce of distilled water, contained

> "... a few drops each of a dilute solution of sodium silicate and dilute phosphoric acid, plus a few grains of ammonic phosphate." (57)

Portions of these solutions were placed in sterilised glass tubes whose necks were sealed immediately. The tubes were heated to 115-130°C for 15-20 minutes and then exposed to diffuse daylight or placed in an incubator that was kept at 30°C. After a few days, some control tubes were opened and the deposits produced by the heat examined; no growth of organisms was observed. However, tubes opened after several weeks or months revealed the presence of numerous organisms (including bacilli, torulae, micrococci and vibriones) on the deposited silica or ferric silicate, although the organisms did not appear to be motile. By varying the conditions, Bastian found that "not too much" sodium silicate must be present and that the solutions must be "faintly acidic or neutral" (58)*.

Many more experiments of a similar nature were described, but all share the same striking feature: no carbon source was ever present in the starting solutions. It must be assumed, therefore, either that Bastian succeeded in creating life based on silicon, which is unlikely in view of the chemical properties of that element**; or that the presence of microorganisms in the tubes was the result of contamination; or that the corpuscles observed by Bastian were not living organisms at all, but inorganic colloidal bodies, which are readily formed on mixing silicates and other salts in solution. Bastian himself showed no awareness that there might be a serious problem here*** and innocently gave his final chapter the title "Does Silicon, either Wholly or in Part, Enter the Place of Carbon into the Composition of the Protoplasm of the

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*The vagueness of these descriptions is characteristic of Bastian's writings.

**The Si-Si bond (42 kcal/mole) is less stable than the C-C bond (80 kcal/mole) and Si does not form polymers as readily as carbon. In addition, chains of silicon are unstable in water and in ammonia. Si does not form multiple (e.g. Si=Si) bonds easily. Finally, Si reacts readily with oxygen to form solid $SiO_2$ (quartz) which does not react further with other molecules, unlike $CO_2$ (59).

***A similar problem had arisen in Bastian's work before. In 1870, Huxley wrote: "Nor does Dr. Bastian's chemical criticality seem to be of a more susceptible kind. He sees no difficulty in the appearance of living things in potash-alum, until Dr. Sharpey puts the not unimportant question, whence did they get their nitrogen? And then it occurs to him to have the alum analysed and he finds ammonia in it." (60)

Organisms Found in the Tubes?" (61). He concluded that no definite answer to this question could be given yet but that it was likely that a partial substitution of silicon for carbon had taken place. (It is not clear, if the substitution was only partial, where the remaining carbon had come from.)

This, then, was Bastian's definitive solution of the problem of the origin of life. As he had already announced in the Preface to The Origin of Life, it was no longer necessary for the evolutionists to postulate long time-spans for the transformation of inorganic into organic matter and the organisation of the latter into living organisms (62). Archebiosis was an every-day occurrence, resulting from the molecular properties of the constituents of living things. Bastian was unable to define these molecular properties; he thought that it was up to the chemist and the physicist to investigate such matters. However, at the time of Bastian's investigations, organic chemistry had advanced sufficiently for him to be able to know, had he been interested in the subject, that organic syntheses require clearly defined conditions which can vary considerably from case to case. In order to synthesise even relatively simple compounds, let alone more complex ones such as proteins, it is not enough simply to mix some inorganic components together, especially if the mixtures do not include a carbon source. In addition, by the beginning of the 20th century the complexity of microorganisms was widely recognised and the onus was on Bastian to explain how this complexity could arise so readily in simple mineral solutions. The time was long past when purported demonstrations of spontaneous generation could carry much weight; assertions of the occurrence of heterogenesis or archebiosis had to be backed up with more detailed theories, be they chemical, physical or biological.

Over the years, Bastian's work revealed a distinct lack of theoretical development, a poor insight into organic chemistry, colloid chemistry and biochemistry, and considerable confusion on the concept of the uniformity of natural processes*. It is not surprising, therefore, that Bastian's later work on spontaneous generation was largely ignored by his contemporaries and by his successors. In his obituary in Nature, Bastian was called

> "...the last of a distinguished band of men of science, which number among its members Pasteur, Darwin, Huxley and Tyndall..." (63)

At the same time, the author of the obituary pointed out that few had cared to follow Bastian's work on archebiosis, which could not be said to have been confirmed. In so far as it is impossible to prove that spontaneous generation can never occur, Bastian may have had logic on his side. But natural science does not proceed by logic alone and Bastian was very much alone, certainly in his later years, in denying that the

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*Bastian frequently confounded the uniformity (or time-invariance) of natural laws with uniformity of initial conditions. The uniformity of natural processes or natural phenomena that he relied on so heavily could only be ensured by the action of the same laws under uniform initial conditions. In addition, Bastian's concept of a natural law left something to be desired on occasion, for example when he wrote that the assumption that some species of microbes might resist temperatures higher than 100°C would violate the principle of the uniformity of natural laws (see p.33 above).

concept of spontaneous generation had become redundant for the explanation of contagious disease and fermentation. In the next chapter it will be shown that the concept was also theoretically redundant to those who aimed to explain the origin of life on earth in evolutionary terms.

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52. H.C.Bastian, The Origin of Life, p.7

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59. See C.Ponnamperuna, The Origins of Life, London, 1972, Ch.10: The fitness of carbon

60. T.H.Huxley, Nature, 2 (1870) 473, op.cit.

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# CHAPTER II
# EVOLUTION AND THE ORIGIN OF LIFE: A NATURAL TRANSITION

Charles Darwin's theory of evolution provided biologists with an explanation of the history of life on earth by natural causes. The concepts of natural selection and of the inherent variability of living organisms served to explain the survival of those varieties that were best adapted to a particular environment at a given time, thus removing the need for explanations in terms of divine creation or supernatural forces. This feature made Darwin's theory particularly attractive to those who held that all vital phenomena are natural processes subject only to natural laws and that there is no epistemological discontinuity between the living and the non-living realms.

It was soon pointed out, however, that Darwin's theory did not account for the entire history of life on earth: it did not explain its origin. Darwin had posed the question by implication in so far as his theory demanded that all living organisms had ultimately descended from a very small number of prototypes, or even from a single primordial organism. Darwin did not, however, explain how the latter might have come into being on a once lifeless earth*.

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*According to the Kant-Laplace theory of the nebular origin of the solar system, which was widely accepted at the time, the earth itself had gone through a process of development and geological conditions had altered drastically since its early history. In particular, the earth's surface was once far too hot to sustain life and it was generally agreed that living organisms could only have survived once the surface of the earth had cooled down to well below the boiling point of water.

From the mid-1860s onwards, numerous attempts were made to remedy this state of affairs and various types of hypotheses on the origin of life were proposed. In this chapter those hypotheses that approached the problem from an evolutionary standpoint will be discussed, their common feature being that they accounted for the beginnings of evolutionary history in terms of a natural transition from non-living to living matter.

Extending evolution backwards

In the final passage of the Origin of Species, Darwin wrote that life was originally "breathed into a few forms or into one..." (1). This choice of words caused some confusion, the notion of the breath of life being traditionally associated with a divine Creator. A number of Darwin's followers were concerned in case Darwin wished to leave open the possibility of a supernatural origin of life, a position which was held to be inconsistent with the philosophical basis of the theory of evolution (2). However, in 1863 Darwin wrote to Joseph Hooker that he had really meant to convey that life had "appeared" by some wholly unknown process, adding

> "It is mere rubbish, thinking at present of the origin of life; one might as well think of the origin of matter." (3)

Yet he did not remain entirely averse from speculating on the subject, as indicated by the following passage from another letter written by Darwin to Hooker, in 1871:

> "It is often said that all the conditions for the first production of a living organism are now present, which could ever have been present. But if (and oh! what a big if!) we could conceive in some warm little pond, with all sorts of ammonia and phosphoric salts, light, heat, electricity, &c., present, that a proteine

> compound was chemically formed ready to undergo still more complex changes, at the present such matter would be instantly devoured or absorbed, which would not have been the case before living creatures were formed." (4)

This statement suggests that Darwin believed that a formation of complex organic matter from inorganic starting compounds was a prerequisite for the primordial generation of living organisms. Moreover, he pinpointed the reason why such a primary formation and subsequent transformation of organic matter is no longer observed in nature: any organic matter newly formed in nature now would be rapidly devoured by pre-existing organisms. Darwin's awareness of the seemingly paradoxical fact that the formation of those chemicals that are required for the generation of life could only have taken place under lifeless conditions puts him far ahead of his contemporaries, none of whom provided a concrete answer to the question why the transition from the non-living to the living is not observed in nature today.

Among Darwin's followers, many were prepared to extend the evolutionary approach to developments leading to the first appearance of life on earth. In an address delivered to the British Association for the Advancement of Science in 1870, Thomas Huxley (1825-1895) stated his belief that protoplasm might have evolved from non-living matter at some stage during the earth's history (5). The main subject of Huxley's address was Pasteur's work on spontaneous generation or "abiogenesis", the term coined by Huxley to denote the generation of living from non-living matter*. Huxley greatly admired Pasteur's experiments and agreed with the conclusion that all known forms of life arise by biogenesis, that is, are derived from other organisms. Nevertheless, he did not wish to reject the possibility that abiogenesis could have taken place in the past under the special physicochemical conditions of the early earth (6). While Huxley characterised his opinion on this subject as no more than an "act of philosophical faith", he took the precaution of warning any potential critics of his views:

> "I think it would be the height of presumption for any man to say that the conditions under which matter assumes the properties we call "vital" may not, some day, be artificially brought together." (7)

Huxley's act of faith was based on his view that protoplasm is the physical substratum of all vital phenomena** In 1868, he had presented a popular exposition of the protoplasmic theory of life***, arguing that all features of living organisms,

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*Huxley did not make a chemical distinction between inorganic and organic non-living matter.

**In his lecture on abiogenesis, Huxley made no mention of Bathybius haeckelli, the "organism" discovered and named by him in 1868 (8). Microscopic examination of specimens from the bottom of the Atlantic Ocean had revealed to him granular and viscous masses which, he believed, represented undifferentiated protoplasm, or "Urschleim". He believed that he had discovered an exceedingly simple organism but was careful not to speculate about its origin. This caution proved justified seven years later, when chemists found that Bathybius was an inorganic precipitate of calcium sulphate, precipitated by the alcohol that had been used as a preservative. Huxley immediately admitted his error. (For a review of the Bathybius case, see ref.9.)

***The background and ramifications of the protoplasmic theory, in particular its interrelations with the cell theory, have been discussed by Gerald Geison (10).

including human consciousness, were the outcome of the nature and disposition of the molecular constituents of protoplasm (11). Moreover, he contended that the formation of living protoplasm was a natural physicochemical process. Protoplasm could be built up from lifeless substances such as water, carbonic acid and ammonia, for example by plants*, and these substances had in turn been formed from the elements carbon, hydrogen, oxygen and nitrogen. There was no break in this series of steps and, in Huxley's opinion, it would be a grave error to assume that a mysterious "vitality" somehow entered the matter of life during the course of such processes. Giving the synthesis of water as an analogy, Huxley observed that the properties of water are radically different from those of either hydrogen or oxygen. This fact did not, however, warrant the assumption that

> "...a something called 'aquosity' entered into and took possession of the oxide of hydrogen as soon as it was formed, and then guided the aqueous particles to their places in the facets of the crystal, or amongst the leaflets of the hoar-frost." (12)

The conviction that the philosophical status of vitality is no better (and no worse) than that of, say, "aquosity" and that there is an unbroken continuum between the living and the non-living formed the foundation for Huxley's conclusion that protoplasm first arose from inorganic matter.

A similar conclusion was reached by the physicist John Tyndall (1820-1893) in a controversial address delivered to the

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*Huxley did not know that organic synthesis by plants requires the action of a highly complex apparatus of enzymes already present in the plant. Although this does not detract from his argument here, Huxley's example has no bearing on the prebiotic formation of organic, let alone living, matter.

British Association in 1874 (13). Tyndall argued that all natural phenomena could, and ought to be, explained in terms of the properties of matter. Tracing the line of life back into the past, he applied this principle to the origin of life and assumed that life arose from inorganic matter by purely physical causes. Life, like everything else, was immanent in matter. In a reply to one of his many critics, Tyndall stressed that science recognised an unbroken causal connection between past and present (14). To account for the transition from a molten, lifeless earth to its present condition, it was therefore necessary to assume that the molten earth contained within it the constituents of life and that these combined into living organisms as the planet cooled. Elsewhere Tyndall wrote that the theory of evolution was incomplete unless one assumed that organised, living matter had originally arisen from inorganic matter (15). He felt that it was inconsistent to believe in evolution and at the same time reject abiogenesis, and while proof for the latter was as yet wanting,

> "There does not exist a barrier possessing the strength of a cobweb to oppose to the hypothesis which ascribes the appearance of life to that 'potency of matter' which finds expression in natural evolution." (16)

Neither Huxley nor Tyndall suggested how the process of abiogenesis might have taken place on the primaeval earth. Their statements seem to imply that inorganic compounds organised themselves into living organisms without any intermediary steps. In contrast, Herbert Spencer (1820-1903) envisaged a complex and prolonged series of events preceding the generation of the first organisms on earth and stressed that the evolution of living forms was only possible after a long evolution of organic matter (17). However, Spencer did not discuss the question of the origin of life in detail. Like most British evolutionists of the day who confronted the problem of the origin of life at all (and most of them preferred to evade the question), Spencer refrained from speculation beyond stating his belief in a gradual transition from the non-living to the living.

Haeckel's solution

The situation was somewhat different in Germany, where a speculative tradition in biology was more firmly embedded, starting with *Naturphilosophie*. The mechanist reaction against *Naturphilosophie* and the materialist reaction against transcendental philosophy combined to give rise to the scientific materialism of the 1850s, exemplified by the work of Ludwig Büchner (1824-1899), Jacob Moleschott (1822-1893) and Karl Vogt (1817-1895)*. Despite their advocation of the empirical method (19), the *Weltanschauung* of the scientific materialists was a metaphysical one; their ideas on such elusive problems as the nature of consciousness and the origin of life were based more firmly on *a priori* considerations than on empirical evidence. Vitalism and idealism were cast out, but speculation remained. This feature is also prominent in the work of Ernst Haeckel (1834-1919), the most prolific writer on the subject of

*An analysis of the life and work of the scientific materialists is presented in Frederick Gregory's *Scientific Materialism in Nineteenth Century Germany* (18).

the origin of life in the late 19th century.

Haeckel was one of the first and most ardent protagonists of Darwin in Germany and it was Darwin's theory rather than philosophical materialism that formed the starting-point for the monistic philosophy erected by Haeckel*. According to Haeckel's monism, all natural processes stand in material, historical and causal connection. On this view of the unity of nature, there could be no fundamental distinction between the living and the non-living world and the denial of such a distinction formed the basis of Haeckel's writings on the origin of life.

Haeckel first treated the problem of the origin of life in detail in two major works on general biology, <u>Generelle Morphologie der Organismen</u> (General morphology of organisms), first published in 1866, and <u>Natürliche Schopfungsgeschichte</u> (Natural history of creation), first published in 1868. Here Haeckel supported his view of the continuity between the inorganic and the organic world with the following observations: (i) All elements found in living organisms are also present in the inorganic domain. (ii) The combinations that are peculiar to living organisms are complex protoplasmic substances, in particular the proteins. (iii) The phenomena of life are physicochemical processes based on the properties of proteins. (iv) The only element that is capable of building up proteins

*Darwin's demonstration that evolutionary history and the apparent purposiveness of living organisms could be explained in terms of natural causes convinced Haeckel of the essential unity of nature. Haeckel's monism will be examined in greater detail in Chapter VI of this thesis.

(in combination with H, O, N, P and S) is carbon. (v) These protoplasmic carbon compounds differ from most other chemical combinations by their intricate molecular structure, their instability and their viscid consistency (20). On this basis, Haeckel constructed his "carbon theory", which stated:

> "The peculiar chemico-physical properties, and especially the semi-fluid state of aggregation, and the easy decomposability of the exceedingly composite albuminous combinations of carbon, are the mechanical causes of those peculiar phenomena of motion which distinguish organisms from anorgana, and which in a narrow sense are usually called 'life'." (21)

To Haeckel, this "theory" was of the utmost importance to one of the most fundamental problems of biology, that of the origin of the first organisms. Darwin's theory of evolution had left this question unanswered and Pasteur's refutation of spontaneous generation was irrelevant to the problem: in Haeckel's view, Pasteur's results had no bearing on the possibility of a generation of "homogeneous, structureless primitive organisms" long ago, organisms that had long since died out. In addition, the classical experiments on spontaneous generation, including Pasteur's, were concerned with the appearance of organisms in organic infusions, consisting of matter derived from pre-existing, decayed organisms. This type of spontaneous generation, or "plasmogony", was of no interest in relation to the appearance of the first living systems on a lifeless earth. What needed to be considered, according to Haeckel, was a hypothesis of "autogony", in other words, a hypothesis

> "...which asserts the direct transition from inorganic substance into individualised organic substance, a

> process that is absolutely analogous to the crystallisation of inorganic matter." (22)*

Haeckel believed that the only difference between autogony and other types of crystallisation was that the type of combinations formed by carbon are neither solid nor liquid, but in a semi-fluid or viscid state. Hence, the aggregates of carbon compounds had a greater inner mobility than solid inorganic crystals. As a result the former, unlike the latter, could grow towards the inside by intussusception as well as outwards by apposition of material from the medium, and could adapt and change internally. Hence, the aggregates would become ever more complex and eventually develop into the simplest organisms known to Haeckel, the Monera. The class of the Monera had been introduced by Haeckel on the basis of his extensive research on unicellular organisms. He placed the ancestors of the Monera before the point of differentiation into plants and animals in phylogenetic history**. The Monera exhibited all vital activities, namely irritability, sensitivity, mobility, nutrition, growth and propagation by division; yet they did not reveal (to Haeckel) any inner structure or

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*"...welche den unmittelbaren Uebergang anorganischer Substanz in individualisirte organische Substanz behauptet, ein Process, der der Krystallisation der Anorgane durchaus analog ist." Haeckel's distinction between plasmogony and autogony is analogous to that between heterogenesis and abiogenesis (or Bastian's archebiosis), respectively.

**Haeckel later distinguished between the Phytomonera, which could build up organic matter from inorganic combinations, and the Zoomonera, which had no such powers of assimilation but fed on organic matter derived from other organisms. The first organisms on earth, the hypothetical Probionta, were included in the class of the Phytomonera (see <u>The History of Creation</u>, p.67).

morphological differentiation. Haeckel believed that the Monera were composed of a single chemical substance, albeit one that probably had an extremely complex molecular structure. Haeckel assumed that the first living organisms on earth were such

> "...homogeneous, structureless, formless lumps of protein or Monera, similar to a Protoamoeba..." (23)*

The primordial Monera arose by autogony as a result of forces inherent in matter present in the primaeval seas. Their subsequent history was outlined by Haeckel as follows. As the individual Monera grew, they began to multiply by simple division as soon as they had grown too large to be stable. Many generations of Monera could have inhabited the seas of the cooled earth before any differentiation of the "lumps of protein" took place. According to Haeckel's theory of plastids (24), the following types developed by simple physicochemical differentiation of the first Monera or "simple cytods", which alone could have arisen by autogony: (i) Enclosed cytods, consisting of particles of plasma surrounded by a membrane. These arose out of simple cytods by the physical condensation of the outer layer of plasma or by the chemical deposition of a covering. (ii) Simple cells, composed of particles of plasma with a nucleus. These arose out of simple cytods by the condensation of the inner plasma into a kernel. (iii) Enclosed cells, which had a nucleus and were surrounded by a membrane and which arose either from enclosed cytods or from simple cells. All subsequent forms of life

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*"...homogene, structurlose, formlose Eiweissklumpen oder Monera, gleich einer Protamoeba..."

arose from the four fundamental plastids (simple and enclosed cytods, simple and enclosed cells) by natural selection, by adaptation, and by differentiation and transformation.

Haeckel believed that his hypothesis on the origin of life bridged the gap between the Kant-Laplace theory on the formation of the earth and Darwin's theory of evolution, and hence provided further theoretical support for the unity of nature. He admitted that his hypothesis was not yet susceptible to experimental verification, one of the major stumbling blocks being that the spontaneous formation of complex carbon compounds such as proteins had never been observed. Nevertheless, Haeckel was optimistic that advances in organic chemistry would lead to the artificial synthesis of proteins and possibly of individualised lumps of protein similar to simple Monera. A second difficulty was the fact that very little was known concerning the physical and chemical conditions of the earth during the period when life made its first appearance, especially as Haeckel felt that the primaeval conditions must have been very different from the present ones. In fact, Haeckel attempted to turn this point to his advantage, pointing out that it could not be disputed that autogony, even if it no longer occurs today, might well have taken place under very different conditions. Hence, even if the past occurrence of autogony could not be verified, it could not be refuted either:

> "We admit that this process, as long as it is not directly observed or repeated by experiment, remains a pure hypothesis. But I must again say that this hypothesis is indispensible for the consistent completion of the non-miraculous history of creation, that it has absolutely nothing forced or miraculous

> about it, and that certainly it can never be positively refuted." (25)

In fact, for some time Haeckel believed that support for his hypothesis of autogony might be drawn from Huxley's discovery of _Bathybius_. To Haeckel, this discovery amounted to a demonstration that the sea bottom is covered with protoplasm that is barely "individualised", strongly reminiscent of the hypothetical _Urschleim_ (primordial slime) of _Naturphilosophie_ (26). Haeckel suggested, reasonably cautiously, that protoplasm might perhaps still be generated continuously from inorganic matter in the special environment of the depths of the sea. Haeckel later accepted that _Bathybius_ itself was an inorganic artefact, but was adamant that this observation had no bearing on the reality of other Monera, some of them as primitive as _Bathybius_ had appeared to be (27).

Haeckel's bold attempt to present a scientific explanation of the origin of life represents an important stage in the history of the problem although it is clear in retrospect that he greatly underestimated the difficulties of his theory. He postulated a number of steps but was unable to suggest any detailed mechanism whereby each step might have taken place. At the time the hypothesis was presented no part of it was testable by experiment and resorting to "unknown conditions" was a hindrance rather than a help in this respect. Now that the structure of numerous proteins has been elucidated and the laboratory synthesis of many proteins has been achieved, it is evident that Haeckel's suggestion of a spontaneous "crystallisation" of simple carbon compounds into protein was a gross oversimplification.

Of course, Haeckel cannot be blamed for ignoring facts that were simply not known at the time, such as the intricate structure of proteins and the biochemical complexity of micro-organisms. Nevertheless, it is surprising that a scientist who was convinced that all vital phenomena are the outcome of changes at the chemical level only paid lip service to the possible chemical complexity of his "lumps of protein". Haeckel was, however, by no means unique in this respect and his views on protoplasm as the basis of life were no more vague than those of his contemporaries.

A more serious criticism concerns the fact that Haeckel did not, at this stage, describe the beginnings of life as a process involving a long series of different stages taking place over a vast period of time. This again is surprising for such an ardent supporter of the evolutionary idea who held that

> "...the world is nothing else than an eternal evolution of substance..." (28)

Autogony was presented as a single physicochemical process, a view which has been criticised by Oparin as being even less plausible than if, in the midst of inorganic matter, a large factory, complete with smoke stacks, pipes, boilers, ventilators, etc., suddenly sprang into existence by some natural process* (29). Analogous criticisms were made by some of Haeckel's contemporaries, in particular by Carl Nägeli

*The phrase "suddenly sprang into existence", the one used by Oparin, is somewhat unfair as Haeckel nowhere presented autogony as a <u>sudden</u> event.

and August Weismann (see below) and Haeckel modified his theory in response. In The Riddle of the Universe, first published in German in 1899, Haeckel described the origin of life as a process that took place in two distinct phases: a phase of autogony, during which inorganic matter was transformed into organic matter of ever-increasing complexity, and a phase of plasmogony, during which the organic matter organised itself into primitive Monera (30). In a more detailed account of the problem, he later emphasised that the generation of life must have been an extremely slow process, taking place over an immense time-span, and incorporated Pflüger's ideas on chemical evolution (see below) to account for the formation of protein (31).

It is easy to criticise Haeckel's theory on the origin of life for its errors and it is impossible to agree with his claim that the riddle of the origin of life had been "answered decisively by our modern theory of evolution" (32). However, Haeckel's writings on the subject firmly placed the problem of life's beginnings in an evolutionary context and he provided his contemporaries with a framework that could be adapted in the light of new knowledge. It was thus that his work was appreciated and Max Verworn (1862-1921), for example, credited Haeckel with having

> "...removed from the early absurd ideas of spontaneous generation their sound kernel and of having transferred it to a purely scientific soil." (33)

Attempts to adapt Haeckel's theory were made by Carl Nägeli (1817-1891) and August Weismann (1834-1914) in the 1880s. As Weismann's theory was largely derived from that of Nägeli, the two will be discussed together.

According to Nägeli, the origin of the living from the non-living was not in the first instance an experimental problem, but a fact that follows from the laws of conservation of matter and force. Organisms must be built up from, and eventually decompose into, materials that are constituents of inorganic nature and

"To deny the Urzeugung is to declare miracles." (34)*

Similarly, Weismann stated that the assumption of abiogenesis is a "logical necessity" (35). Both authors pointed out that it could not, however, be assumed that life on earth arose at once in any form known to us now; it must have developed gradually over an immense period of time. Furthermore, the first organisms must have been utterly simple and devoid of any differentiation. To Nägeli and Weismann, Haeckel's view that the first organisms were Monera, similar to the simplest organisms known today, was untenable. The simplest known Monera were not homogeneous, they were of considerable size, and showed a highly developed mobility. These facts suggested that present-day Monera had evolved by a historic process, a long phylogenetic development, and that their simplicity was only apparent (36). In fact, it was likely that the type of organism that could arise by abiogenesis was so small as to be undetectable under the microscope. Nägeli proposed that it was "a small drop of homogeneous plasma" ("ein Tröpfchen von homogenem Plasma" (37)), composed

*"Die Urzeugung leugnen heisst das Wunder verkunden." For a discussion of the term Urzeugung, see Introduction, pages 15,16.

only of protein. Hence, the hypothesis of the Urzeugung presupposed the spontaneous formation of protein. The synthesis of protein had not yet been achieved by organic chemists, nor had its formation in free nature been observed, but there was no reason to believe that protein could not be built up spontaneously. According to Nägeli, the process goes unobserved because it probably takes place just under the surface layer of a fine porous substance such as clay or sand, where the molecular forces of solid, liquid and gaseous substances cooperate*. Once proteins were formed they would organise themselves into micellae and a whole network would be built. Subsequently, this mass of plasma ("Plasmamasse") would gradually form an orderly arrangement due to forces inherent in the protein molecules themselves:

> "The originally disorderly arrangement brought about by external conditions must eventually change into one that is ordered and solely determined by the nature of the protein micellae....The properties of the organised substance are determined by the mutual disposition of the micellae and by the physicochemical interactions between them." (39)**

The organised substance formed in this second phase was the simplest living unit, called "probiont" by Nägeli. In conclusion, Nägeli divided the events leading to the generation of life into two distinct phases: the formation

*It should be noted that Nägeli implied that proteins are still formed in nature. Weismann, on the other hand, applied Nägeli's hypothesis on protein formation to the prebiotic era only (38).

**"Die ursprüngliche regellose oder von äusseren Umstanden bewirkte Anlagerung muss zuletzt in eine geordnete und bloss von der Natur der Eiweissmicelle bedingte Übergehen.... Die Eigenschaften der organisirten Substanz werden bedingt durch die Zusammenordnung der Micelle und durch die physikalisch-chemischen Vorgänge zwischen denselben."

and accumulation of protein matter and its organisation into micelles, and the development of probionts from this micellar mass of plasma.

Weismann was similarly led to conclude that the substance of even the simplest living organisms consists of fundamental vital units, which he called "biophors", or carriers of life (40). He believed that existing organisms are composed of many different kinds of biophors that arose by multiplication. Originally, however, they arose from non-living matter and were independent organisms ("biophoriden"). Later these biophoriden formed colonies and underwent differentiation. Weismann did not know precisely how the biophors, composed simply of protein, first came into being, but regarded Nägeli's hypothesis as the most attractive one.

The hypotheses of Nägeli and Weismann went beyond that of Haeckel only in so far as they revealed a greater recognition of the complexity of existing microorganisms. It is true that this complexity was understood only in the vaguest terms, but the realisation that any degree of functional complexity can only have arisen by a long evolutionary process constitutes an advance over Haeckel's ideas on this point. On the other hand, the idea that cells and organisms are made up of simple living units is no longer tenable. The vital properties of any organism are those exhibited by the organism as a whole and result from the complex interaction of its constituent parts. To say that any of these parts in isolation are the carriers of life is an oversimplification of the integrated functioning of living organisms. In addition, Nägeli and

Weismann still believed, with Haeckel, that the first organisms were small lumps of protein, an over-simplification that continued to be made for many years to come. Again like Haeckel, Nägeli and Weismann were unable to propose a detailed mechanism whereby protein could have been formed from inorganic matter.

The concept of chemical evolution

In the meantime some attempts had been made to account for the primordial formation of protein by specific chemical mechanisms. The first proposal in this direction was made by the physiologist Eduard Pflüger (1829-1910), renowned for having established that respiration is an intracellular process. His detailed views on the chemical and biological properties of proteins, which he considered to be the essence of the living process, are described in one of his classic papers on respiration, published in 1875 (41). In this paper Pflüger drew a distinction between dead, or storage, protein ("todtes Eiweiss") and live, or protoplasmic, protein ("lebendiges Eiweiss"). Dead protein was stable and chemically inert while live protein was extremely labile and highly oxidisable. According to Pflüger, the lability of "live protein" was the basis of all chemical metabolic transformations in the living cell.

The fundamental difference between dead and live protein was at the chemical level and Pflüger believed that he had discovered the nature of this difference. In an investigation of the nitrogenous breakdown products of protein, he found that the decomposition of "live" proteins yielded substances such as urea, hypoxanthine, guanine and creatine, which all contain "cyanogen" (the CN-radical). He never obtained such products upon the artificial cleavage of "dead" protein and Pflüger concluded that live protein is characterised by the presence of cyanogen. He suggested that in the formation of cellular (live) protein from food (dead) protein, the latter undergoes a change resulting from the reaction between carbon and nitrogen atoms to form cyanogen. Such a reaction was known to be associated with the absorption of large amounts of heat and the high energy content of the cyanogen radical could explain the high degree of lability of live protein.

According to Pflüger, the CN-radical formed the link between the non-living and the living world, and any account of the origin of life had to explain how cyanogen was generated. Pflüger pointed out that, in the laboratory, cyanogen compounds are formed when nitrogen gas comes into contact with red-hot coal or when a lightning discharge is passed through nitric acid. He concluded that cyanogen compounds could therefore have formed easily when the earth was still glowing hot. Simple hydrocarbons were also known to be formed at high temperatures; for instance, methane and ethylene could be made by passing carbon sulfide or hydrogen sulfide over glowing metals. Finally, simple aromatic compounds could be synthesised in the laboratory at high temperatures. Hence,

> "One sees how all the facts of chemistry point quite strongly and remarkably to fire as the force that has produced the constituents of proteins by synthesis. Life therefore originates from fire and, in its fundamental aspects, was formed at a time when the

earth was still a glowing ball of fire." (42)*
According to Pflüger's theory, cyanogen compounds were formed during the early stages of geological history and were gradually transformed during the immeasurably long period when the earth's surface cooled to its present temperature. The compounds underwent polymerisation and reacted with oxygen and, later, with water and salts, eventually forming labile, live proteins. Pflüger's notion of a labile live protein was the outcome of an oversimplified interpretation of metabolic processes. The metabolic transformations of living systems are regulated by the action of a vast number of highly specific enzymes and cannot be explained by the characteristics of a single radical or molecular group. Each enzyme has its own active group, characterised not only by the atoms it contains but also by its steric configuration. Secondly, Pflüger's distinction between live and dead proteins was based on his incomplete knowledge of specific metabolic pathways. Breakdown products such as urea are formed by secondary enzymic reactions and are not the immediate products of protein decomposition. Finally, as pointed out previously, the formation of protein can by no means be equated with the beginning of life.

Yet Pflüger's theory was much stronger than the hypotheses of Haeckel, Nägeli or Weismann. He postulated a testable mechanism whereby certain constituents of living organisms might have been formed and stipulated the type of conditions under which this

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*"Man sieht, wie ganz ausserordentlich und merkwürdig uns alle Thatsachen der Chemie auf das Feuer hinweisen, als die Kraft, welche die Constituenten des Eiweisses durch Synthese erzeugt hat. Das Leben entstammt also dem Feuer und ist in seinen Grundbedingungen angelegt zu einer Zeit, wo die Erde noch ein glühender Feuerball war."

process could have taken place on the lifeless earth. Moreover, these conditions were consistent with the Kant-Laplace theory on the formation of the earth. Another point of interest is Pflüger's realisation that protein synthesis could not have occurred in a single step. The most detailed part of his hypothesis concerns the primordial synthesis of the building blocks of proteins and he explicitly ascribed the formation of protein matter itself to a very much later date. In this respect, Pflüger's views have a much more modern ring than those of his contemporaries, who showed less concern with chemical matters*. Regardless of the details of the theory, it was with Pflüger that the idea of chemical evolution was born, the idea, that is, that the origin of life was preceded by a long process of chemical evolution.

Several variations on Pflüger's theme were presented in the 1880s and 1890s. For example, an alternative mechanism for the primaeval synthesis of proteins was proposed by Pflüger's pupil Oscar Loew (1844-1941) and his colleagues in 1881 (44). Loew objected to the concept of a living molecule or living unit on the grounds that every vital action is the result of the working of a complex machinery consisting of many different molecules. No

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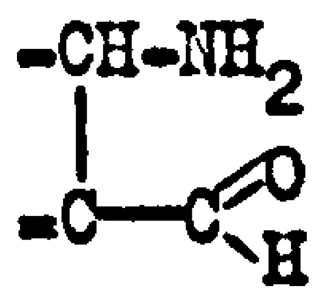
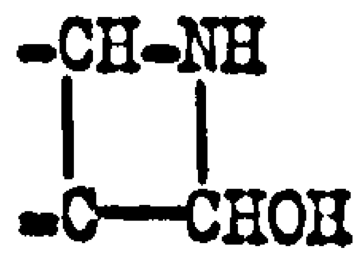
*Pflüger, incidentally, was the first to suggest that carbon dioxide was not the original carbon source in the generation of living organisms, but had to be regarded strictly as a product of the activities of living organisms (43). This view is in accordance with modern ideas on the atmosphere of the early earth. However, the modern view that carbon was originally present in the atmosphere in the reduced form, for example as methane, is based on comparative studies of planetary and stellar spectra. Pflüger reached his conclusion on purely hypothetical grounds, being convinced that the beginnings of life were to be found in cyanogen.

single molecule could be said to be alive and Loew therefore rejected Pflüger's terminology of live and dead proteins. He did, however, accept the idea that proteins represent the chemical basis of all vital phenomena and that the differences between living and dead systems should be sought in a chemical difference between the proteins in the respective systems (45). Loew proposed that a distinction be made between "active" and "passive" rather than live and dead protein, claiming that such a distinction was purely chemical and had no implications regarding vitality at the molecular level.

Loew next presented his mechanism for gradual protein synthesis on the primitive earth; the details are naive and of little interest. According to Loew, the proteins formed on earth originally were passive and stable but became active and labile by their mutual interaction in protoplasm. The chemical difference between active and passive protein resided in a single chemical group, pictured as follows:



active group



passive group (46)

Loew's theory was no great advance over that of Pflüger. Both Loew and Pflüger reduced all vital phenomena to the chemical properties of proteins and, in particular, to one molecular group that supposedly endowed the protein molecule with the lability considered to be essential for life. All objections raised against Pflüger's views apply equally to those of Loew. In addition, Loew's objection to the concept of a living molecule, while sound in principle, loses much of its force in view of the heavy reliance of his hypothesis on the distinction between "active" and "passive" protein.

A third hypothesis was presented by Victor Hensen (1835-1924), who was particularly concerned with the degree of stability of prebiotically formed proteins (47). He accepted Pflüger's idea that simple organic compounds were formed relatively easily when the earth's surface was still very hot. With regard to the synthesis of proteins, however, he wondered whether the newly formed protein was oxidisable by oxygen in the atmosphere, in which case it would be too unstable to undergo further synthetic transformations, or whether it was not oxidisable, in which case it would be too inert. In an attempt to overcome this problem, Hensen drew up a scheme of hypothetical reactions between hypothetical organic compounds. While the significance of his scheme is obscure, Hensen was probably the first to point out the problem of the lability of complex organic compounds in the presence of molecular oxygen. The progressive transformation of organic matter over long periods of time could only have occurred if the breakdown resulting from oxidation was somehow prevented. It was only with the concept of an initially reducing atmosphere that this problem was later overcome.

In Britain, the physiologist F.J. Allen developed views that show some similarities to those of Pflüger (48). Like Pflüger, Allen paid particular attention to the nitrogenous compounds of living organisms. He regarded energy transfer between molecules as the fundamental phenomenon of life and believed that nitrogen plays a crucial role in this energy traffic. Allen did not reduce all vital phenomena to cyanogen or some other molecular group but nevertheless assumed that some active nitrogenous molecule was responsible for metabolism. The nature of this "active molecule of living substance" (49) was not known but Allen assumed that it must be very large although probably not a protein. Allen's ideas on the primordial formation of this living substance were equally nebulous. He postulated an initial accumulation in the terrestrial waters of carbon and nitrogen compounds, possibly formed in the damp air by the action of lightning discharges and swept down in rain. From these raw materials living substance was supposed to have arisen by some unknown mechanism.

There are some features of interest in Allen's work. He paid particular attention to the interactions between organic and inorganic nature and argued that just as the organic world was a product of its inorganic environment, so the living world had shaped the environment. For example,

> "The very atmosphere may be said to be the product, as well as the producer of life; for the carbon dioxide and oxygen, and part (if not all) of the nitrogen, have been given to the atmosphere by the respiration, decomposition and combustion of organic matter." (50)

Nevertheless, Allen did assume that free oxygen had been present in the primaeval atmosphere; he believed that its concentration had been diminished temporarily through the mass production of nitrogen oxides.

Finally, Allen believed that "the first attempts at life" were still continuing in nature but that the process goes undetected because any primitive vital substance would be assimilated by pre-existing organisms before it had the opportunity to develop into full-fledged organisms (51). This idea, which had been expressed earlier by Charles Darwin, did not become common currency until Oparin's theory of 1936 exerted its influence.

Stagnation and the demise of protoplasm

In the early decades of the twentieth century little further progress was made on the question of the origin of life and the reason for this impasse may be sought in the fact that the biological sciences were undergoing a fundamental change in this period, especially with the rise of biochemistry (see below). The subject continued to be discussed, but in qualitative terms. The adherents of the idea that a gradual transition from non-living to living matter had taken place in primaeval times felt that it was only a matter of time before more detailed theories could be formulated. The realisation grew that much progress in the study of the constituents of organisms, especially the proteins, was required first.

The long time-spans involved in the primordial generation of life came to be emphasised more and more*. At the same time, some were optimistic that a better understanding of protein and colloid chemistry would make the synthesis of life in the laboratory a relatively straightforward matter. This was the position taken by Edward Schäfer (1850-1935), for example, in his presidential address to the British Association at their

*Many made an explicit distinction between their views and the old ideas on spontaneous generation on this basis. It was also argued for this reason, for example by Edward Schäfer (52) and Felix le Dantec (53), that Pasteur's work on spontaneous generation, while perfectly valid in its own right, had no bearing on the subject of the origin of life.

meeting in Dundee in 1912 (54). And the French mechanist Felix le Dantec* (1869-1917) expressed his view as follows:

> "When the effective synthesis [of a living cell] is obtained, it will have no surprises in it - and it will be utterly useless. With the new knowledge acquired by science, the enlightened mind no longer needs to see the fabrication of protoplasm in order to be convinced of the absence of all essential difference and all absolute discontinuity between living and not-living matter." (57)

Both Schäfer and le Dantec were arguing from a mechanistic standpoint, an approach that was rejected by Benjamin Moore (1867-1922), who held the first Chair in Biochemistry in Britain, at the University of Liverpool. Moore believed that there was a fundamental distinction between the living and the non-living in terms of the energetic changes exhibited by each class (58). The living cell was primarily a transformer of energy: it transformed chemical energy into "biotic energy", the latter being expressed in the form of specifically vital phenomena such as individual development, reproduction and metabolism. At the same time, Moore argued for a historical continuity between the inorganic and the living world. According to his "law of complexity", the evolution of matter had given rise to ever more complex material structures with

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*le Dantec, who was a pupil of Pasteur, was one of the first French scientists to argue for an origin of life from purely chemical beginnings. The question of life's beginnings on earth had received very little attention in France since Pasteur's victory over Pouchet. Farley has argued that it was the impact of Pasteur's triumph which was also responsible for the cool reception in France of Darwin's theory of evolution (55). To many, the idea that all living organisms had descended from a prototype appeared to imply that this prototype had been generated spontaneously, especially from the precedent of Lamarck's theory of the spontaneous origin and evolution of life. It is certainly the case that a number of biologists in France who defended Darwin's theory at the same time attacked Pasteur and asserted the reality of spontaneous generation (56).

ever more complex functions, resulting eventually in the generation of living things (59)*. It was not enough, however, to consider the origin of the material substratum alone: the evolution of novel types of energy transformations might induce further material development. By way of example, Moore suggested that scientists should look for colloidal systems sensitive to sunlight and investigate whether their photosensitive reactions induced any further structural development (61).

Although Moore's concept of "biotic energy" did little to clarify matters, his emphasis on the complex interactions between structural and functional development is of interest. In the context of biological evolution, many accepted that the evolution of new functions, such as sexual reproduction, might create new conditions which favoured the further evolution of organisms. This concept had not, however, been applied previously to the events leading up to the origin of life. Like most others, however, Moore had little to offer in terms of specific mechanisms and the question must be answered why the problem of the origin of life remained so elusive.

By the turn of the century, the protoplasmic theory of life had lost its heuristic value. The idea that a single, if complex, chemical substance was responsible for all vital phenomena had become untenable with the growing awareness of the complex metabolic interactions of living cells. The question of the origin of life, however, continued to be discussed in terms of

*Moore, incidentally, was the first, I believe, to use the term "chemical evolution" (60).

the origin of protoplasm, vital substance or a colloidal mass for some time. The chemist H.E. Armstrong wrote a devastating critique of the misplaced optimism* with which biologists continued to debate the subject in terms of vague generalisations and old-fashioned notions such as protoplasm, which he characterised as "the convenient cloak of an appalling amount of ignorance" (63). He pointed out that while many biologists seemed to agree that the origin of life was at root a chemical problem, they rarely invited the participation of chemists in their discussions of the subject, adding

> "It is clear that, so long as biologists are satisfied with the modicum of chemistry which is now held to serve their purpose, they will never be able to escape from the region of vague surmise." (64)

Five years earlier, in 1907, a renewed cooperation between chemists and biologists had been advocated by the protein chemist Emil Fischer (1852-1919), but from the opposite point of view (65). Fischer argued that organic chemistry, which originally had been concerned with the study of natural organic compounds of animal and vegetable origin, had become divorced from its biological roots in the latter half of the 19th century. The study and synthesis of thousands of artificial organic compounds had been extremely fruitful for the development of experimental methods and the elaboration of theories. According to Fischer, the time had come, however, for organic chemists to renew their cooperation with biologists and concern themselves with functional matters, especially with biochemical processes.

*He wrote sarcastically of Benjamin Moore, "brimming over with biotic energy". (62)

In fact, it was biochemistry that was to provide a fresh stimulus to the field. As has been argued convincingly by Robert Kohler, the emergence of biochemistry as a distinct discipline around the turn of the century coincided with the acceptance of the view that life was "a self-regulating dynamic equilibrium of catalytic reactions" (66). The enzyme theory of life replaced the protoplasmic theory and the study of enzymes and their role in metabolic reactions became an active and rapidly expanding field. The findings of biochemistry did not have an immediate impact on the question of the origin of life. As the living cell revealed more and more of its complexity, the question of its origins became more and more difficult. Much had to be learned before fruitful questions on the origin of life could be asked. In fact, even in recent years one eminent biochemist, Erwin Chargaff, characterised the problem of the origin of life as "truly a subject for the scientist who has everything" (67).

The impact of biochemistry on the problem will be examined in Part II of this thesis. Before then, a number of hypotheses that were proposed as alternatives to the evolutionary idea of a transition from non-living to living matter need to be discussed.

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## CHAPTER III
## LIFE FROM SPACE ?
## THE THEORY OF COSMOZOA OR PANSPERMIA

The evolutionary approach to the problem of the origin of life, discussed in the previous chapter, was based on the assumption that life is an emergent feature of the universe. In contrast, the most influential rival hypothesis in the latter half of the 19th century was founded on the belief that life is an eternal feature of the universe. The adherents of this view imposed a rigid interpretation on Pasteur's results on spontaneous generation and accepted that life is necessarily antecedent to life. Life in the universe had no beginning on this view, but life on earth had a definite origin in time. According to the Kant-Laplace hypothesis, the earth itself had not existed for eternity, but evolved from a mass of gases, and could not have sustained life during its early history. Given these limitations, it was concluded that, once conditions on earth were ripe, life had reached the planet from outer space in the form of a seed, germ or spore. The hypotheses based on this concept did not, therefore, concern themselves with the question of the origin of life _per se_ but with possible mechanisms for the transfer of living organisms from planet to planet and with the question of how these organisms could survive their journey through space. While the idea that living seeds ("spermata") are ever present in the universe goes back at least to the Presocratic philosopher Anaxagoras (5th century BC), this modern version of the panspermic hypothesis was founded by Hermann Richter in 1865.

Richter's theory of cosmozoa
Hermann Eberhard Friedrich Richter (1808-1876) was born and educated in Leipzig, where he studied medicine. In 1837 he was appointed Professor of Therapy at the Academy of Surgery and Medicine in Dresden but lost his position in 1849 as a result of his participation in the 1848 revolution (1). From 1850 until his death, he co-edited Schmidt's Jahrbücher der in- und ausländischen gesammten Medicin with A. Winter. In his capacity as editor of this series, he wrote a number of articles reviewing advances in a wide range of scientific fields and explaining their relevance to medicine. One of these articles, published in 1865, dealt with Darwin's theory of evolution (2). Richter praised the success and boldness of Darwin's theory, comparing the idea of a transformation of species by natural selection favourably with beliefs in the divine design of the living world. He felt, however, that the theory was not radical enough in so far as it failed to provide an explanation of the origin of the primordial cell (or cells) from which subsequent life forms had descended. If Darwin imagined that our original ancestors were created by divine intervention his own theory of evolution would be redundant; for a creative force that could bring into being a primordial cell would be equally capable of creating different species and complex organisms. To Richter this was an absurd conclusion as he was convinced that all biological processes could be explained solely in terms of natural laws. At the same time, he found it impossible to envisage how living organisms could have arisen from purposeless inorganic matter without the assumption of some teleological principle

beyond natural law.

In an attempt to overcome this problem, Richter considered the assumptions of what he called the "new astronomy". The imperishability of matter and force implied that the universe could not have been created from nothing. Therefore, the universe had existed for eternity and would never end. All that ever changed was form: new forms arose and old ones disappeared in never-ending succession. It followed, according to Richter, that space was full of growing, mature and dying celestial bodies ("werdenden, reifen und absterbenden Weltkörper"), the mature bodies being those that could harbour life. Richter concluded that there had always been some planet on which living organisms were present and that life must be eternal:

> "We therefore also regard the existence of <u>organic life</u> in the universe as eternal; it has always existed and has propagated itself in uninterrupted succession, and indeed <u>in organised form</u> - not as a mysterious Urschleim, but in the form of living organisms, as <u>cells</u> or <u>individuals</u> composed of cells. <u>Omne vivum ab aeternitate e cellula</u>!" (3)*

To the question of how the first organisms had appeared on earth Richter gave the answer: from space. He believed that seeds or germs could travel through space, for instance on the surface of meteorites. If only one such organism fell on a planet with

*"Demnach halten wir auch das Dasein <u>organischen Lebens</u> im Weltreich für ewig; es hat immer bestanden und hat in unaufhörlicher Folge sich selbst fortgepflanzt, und zwar <u>in organisirter Form</u>, nicht als ein mysteriöser Urschleim, sondern in Gestalt lebender Organismen, als <u>Zellen</u> oder aus Zellen zusammengesetzte <u>Individuen</u>. <u>Omne vivum ab aeternitate e cellula</u>!"

conditions suitable for life, it could become the starting point for the evolution of many new forms of life. Darwinian theory was now complete. In Richter's words:

> "This hypothesis is clearand simple; it can be discussed and elaborated in scientific terms; it is consistent with views established in other fields of science; it provides the cornerstone for Darwin's bold edifice." (4)*

The methods by which germs might travel through space were not discussed in great detail by Richter. He mentioned that chemists had demonstrated the presence of carbon in meteorites, which he believed to be almost certainly of biological origin**. He also emphasised the presence of bacteria in the atmosphere, even as high up as in the Alps and the Pyrennees, as had been established by Pasteur and others. According to Richter, it was therefore reasonable to assume that germs floating high in the atmosphere could be trapped by meteorites flying past the earth and subsequently be carried through space. In a later paper, dealing with climatology and meteorology, he elaborated further on this question (6). Here Richter assumed the existence of an

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*Diese Hypothese ist klar und einfach; sie lässt sich naturwissenschaftlich erörtern und ausbilden; sie steht im Einklang mit den auf anderen Gebieten der Naturwissenschaft eingebürgerten Anschauungen; sie liefert den Schlussstein zu Darwin's kühnen Gebaüde."

**In 1871, Richter reported on the chemical analysis of a meteorite that had fallen in Sweden the year before (5). The results, according to Richter, suggested the presence of humus, indicative of the activity of fermenting organisms. To Richter, these findings provided proof for his theory of cosmozoa and for his opinion that any theory of spontaneous generation was superfluous.

atmosphere in so-called empty space ("Weltluft" or "Welt-atmosphäre") from which the earth, like other planets, continuously drew a portion towards itself. The friction between the "Weltatmosphäre" and the earth's atmosphere would cause bits of the latter to be torn off and swept into space continuously. Hence, the earth would leave a trail of polluted air behind, just like a locomotive. The polluted air contained not only gases, but also "dust" of mineral and organic origin, including germs, spores, yeast cells, eggs, larvae, etc. These "carriers of life" ("Lebensträger") would float around in the universe and occasionally fall down on a planet. Similarly, life on earth had developed from a seed derived from another planet inhabited by living organisms.

Richter's theory was not complete. He did not, for example, touch on the problem of how organisms could withstand the hostile conditions of space. Nevertheless, his theory presented a number of attractive features: it removed the problem of spontaneous generation as irrelevant; it could accommodate Darwin's theory of evolution without having to explain the origin of a primordial cell from inorganic matter on a lifeless earth; it did not require any postulates involving supernatural agencies; and by declaring all living forms to have always descended from other living beings, it retained the autonomy of life. Hence, Richter's theory offered an alternative both to the view of living species as divine creations, which had lost much ground especially after Darwin, and to the concept of life as a set of properties exhibited by certain combinations of otherwise lifeless matter, which many regarded as uncomfortably materialistic. As will be argued below, it appears to have been this latter point in particular which impressed some of Richter's most illustrious followers.

Worlds in collision: Sir William Thomson

In August 1871, Sir William Thomson (1824-1907), later Lord Kelvin*, addressed the British Association for the Advancement of Science at their meeting in Edinburgh (7). In his address, Sir William praised inductive empiricism as being the method which had led to so much scientific progress. Giving numerous examples from astronomy and "cosmical physics" in support of this claim, Thomson suggested, however, that the situation was somewhat different in biology. Here a successful methodology had not yet been developed and philosophical errors continued to be made. For example, it was still maintained by some that dead matter could have formed into protoplasm or "germs of life" under environmental conditions different from those encountered on earth today. Thomson continued,

> "But science brings a vast mass of inductive evidence against this hypothesis of spontaneous generation..... Careful enough scrutiny has, in every case up to the present day, discovered life as an antecedent to life. Dead matter cannot become living without coming under the influence of matter previously alive. This seems to me as sure a teaching of science as the law of gravitation." (8)

It could be objected that the inductive evidence against spontaneous generation was obtained under a limited range of conditions, but Thomson strongly rejected the possibility that the situation might have been otherwise under different environmental conditions. Such an assumption was "opposed to all

*For reasons of consistency, the name Thomson will be used throughout.

philosophical uniformitarianism" and the concept of spontaneous generation was "a direct contravention of what seems to us biological law" (9). Life proceeds from life, and nothing but life.

Thomson next considered the question of how life had originated on earth, taking into account the fact that the earth was once a red-hot globe on which no life as we know it could exist. He aimed to find a solution consistent with the ordinary course of nature and not to invoke an "abnormal act of Creative Power". Such a solution could be found by considering the analogy of a new volcanic island that becomes covered with vegetation only a few years after it has sprung up from the sea. In such cases it was generally assumed that the vegetation resulted from seeds that had wafted to the island through the air or sea. Similarly, the beginning of vegetable life on earth might have started with the fall of a seed-bearing meteorite on the planet. But where did these meteorites come from? Thomson believed that collisions between large masses moving through space are common events and that large quantities of debris must be shot forth in all directions as a result. If one of the colliding bodies were an inhabited planet, some of the fragments scattered through space would undoubtedly carry living organisms:

> "Hence and because we all confidently believe that there are at present, and have been from time immemorial, many worlds of life besides our own, we must regard it as probable in the highest degree that there are countless seed-bearing meteoric stones moving about through space." (10)

In other words, life had always existed in the universe and had reached the earth on a meteorite derived from another inhabited planet. In anticipation of any objections, Thomson commented,

> "The hypothesis that life originated on this Earth through moss-grown fragments from the ruins of another world may seem wild and visionary; all I maintain is that it is not unscientific." (11)

It should be added that Thomson was less certain about the processes whereby the arrival of a few seeds on earth had given rise to the endless variety of plants and animals that now inhabit the planet*. He was unhappy with a theory of evolution, "if evolution there has been" (12), based on the concept of natural selection. This concept took into account insufficiently the argument of design according to Thomson and he ended his lecture as follows:

> "But overpoweringly strong proofs of intelligent and benevolent design lie all around us, and if ever perplexities, whether metaphysical or scientific, turn us away from them for a time, they come back upon us with irresistible force, showing to us through nature the influence of a free will, and teaching us that all living beings depend on one ever-acting Creator and Ruler." (14)

This final statement is in marked contrast with Sir William's previously stated intention of not invoking any act of creative power. He was true to his word only in so far as his theory of the appearance of life on earth was a highly mechanical one. While the hypothesis was backed up with methodological arguments, however, it is hard to avoid the impression that it was at least partly inspired by deeper philosophical assumptions regarding the nature of life.

*In a lecture given in 1897, in which Thomson referred to his earlier views on the appearance of life on earth, he went so far as to suggest that "an abundance of seeds of all species of the present day" had been scattered over the earth (13).

Thomson used two methodological arguments. Firstly, the conclusion that life is necessarily antecedent to life was forced on us by the negative results of a vast number of experiments on spontaneous generation, in accordance with the method of inductive empiricism. Secondly, any claim that some form of spontaneous generation might have taken place under different environmental conditions was in conflict with philosophical uniformitarianism. Thomson did not here appeal to uniformitarianism in the strong sense in which it was commonly used by the geologists of his day. The latter assumed that events that had taken place in the past could be inferred from the study of processes still at work. In other words, they assumed that changes in initial conditions had been sufficiently minor to ensure that the same processes were active in the past and the present. Thomson was strongly opposed to this uniformitarian position, especially in view of his calculations of the age of the earth, which suggested that conditions on the planet must have undergone comparatively radical changes since its formation. His "philosophical uniformitarianism", then, was used in the weaker sense of the principle that states that the same causes under the same initial conditions lead to the same effects at all times; in other words, that natural laws are time-invariant. Hence, his argument was that inductive empiricism had established the concept that life can only come from life as a natural law, and philosophical uniformitarianism demanded that this law be invariant.

Not surprisingly, this argument provoked strong criticism. E.R. Lankester (1847-1929) wrote that the empirical evidence in support of Thomson's "pseudo-law" was significantly less substantial than that supporting the law of gravitation (15). Biologists were not now so naive as to look for the spontaneous generation of complex living organisms but were aware of the fact that they ought to be investigating the possibility that simple organic matter may originate de novo. The observations that supported Thomson's statement had no bearing on this question, which had barely begun to be investigated for purely technical reasons.

In Germany, Johann Zöllner fiercely criticised the inductive methodology of Sir William Thomson and other English scientists (16). Thomson's extraordinary reliance on induction in his statements on spontaneous generation was to him indicative of how little familiar some scientists were with the first principles of the theory of knowledge. According to Zöllner, the principle of the intelligibility of nature in causal terms demanded that some form of spontaneous generation could occur under certain, as yet unknown, conditions. Moreover, there were technical objections to Thomson's hypothesis: when meteorites enter the atmosphere of the earth, friction leads to a very large rise in their surface temperature. Therefore, even if a meteorite covered with organisms had reached our atmosphere intact, the organisms would without exception be burnt to death before they reached the earth (17). The entire idea, in fact, was highly unscientific in Zöllner's opinion.

E. Maitland objected to Thomson's statements on the nature of life (18). To speak of life as necessary for the production of life was to assume that we already knew the limits to the productive powers of nature, and to assert that life was not a natural product was to restrict our definition of nature by some arbitrary limit. Was "our dear mother earth" no mother at all, then, but incapable of producing her own children? This concept of a barren earth spoilt what might otherwise have been a "pretty idea" of

> "...the planets as so many orchids in the flowering garden of the Universe, and the meteorites as their fertilising bees..." (19)

Thomson's ideas on the nature of life were firmly based on the argument of design, which also played a role in his opposition against the theory of evolution by natural selection. Loren Eiseley has argued that Thomson's concern with the question of the age of the earth (which, according to his calculations, left insufficient time for evolution to have produced its results by the slow and haphazard mechanism of natural selection) was inspired by an a priori opposition to Darwin's theory on fundamentalist religious grounds (20). In contrast, Sharlin has written that Thomson's main argument against the theory of evolution was that the latter contradicted well-founded theories of physics (21). In a more thorough analysis of Thomson's thought, Burchfield also reached the conclusion that Thomson's interest in geochronology and geological uniformitarianism was based on scientific considerations alone (22). In addition, however, Burchfield emphasised that Thomson regarded the regularity and order of the universe as evidence of the work of a guiding intelligence. While this order was to be understood in terms of universally applicable natural laws, Thomson did believe that a divine alteration in the laws of nature had to be assumed with respect to the creation of life (23).

It appears, therefore, that there was a complex interaction between philosophical, methodological and scientific factors in Thomson's ideas on the nature and development of life. His concern with the age of the earth may have been based primarily on an interest in questions of physics and cosmology, but the result of his calculations, which appeared to imply a refutation of the theory of evolution by natural selection, probably reinforced views of the nature of life which he had arrived at independently, on philosophical grounds. Hence, it is plausible that his hasty rejection of the idea that life might arise from non-living matter under any circumstances was inspired in the first instance by philosophical assumptions regarding the transcendental nature of life. Given the existence of life, it might move about the universe as mechanically as any inorganic object, but the question of its nature and development was beyond mechanics*. Thomson did not justify his claim that life was eternal, but appears to have regarded it as self-evident. As suggested by Sharlin, the idea that life had existed since time

*In 1897, Thomson stated: "Mathematics and dynamics fail us when we contemplate the earth, fitted for life but lifeless, and try to imagine the commencement of life upon it. This certainly did not take place by any action of chemistry, or electricity, or crystalline grouping of molecules under the influence of force, or by any possible fortuitous concourse of atoms. We must pause, face to face with the mystery and miracle of the creation of living creatures." (24)

immemorial was a belief "fit to a mind used to mathematical patterns of thinking" (25).

Hermann von Helmholtz: reductionist or transcendentalist ?

In Germany, the theory of cosmozoa gained popularity, not in the first instance through Richter's work, but through the support it received from the renowned bacteriologist Ferdinand Cohn (1828-1898) and the highly influential physiologist and physicist Hermann von Helmholtz (1821-1894). Cohn's support for the theory was derived from his opposition to the doctrine of spontaneous generation. Likening life to the eternal flame of Vesta, Cohn favoured Sir William Thomson's idea that life on earth had been derived from another inhabited planet (26). He did not accept the mechanism of transfer proposed by Thomson, however, but believed that bacteria could be swept up in air currents and be pushed into space. The cold conditions of space posed no problem, because experiments had shown that many bacteria retain their germinating power after having been frozen at -18°C for "many hours" (27). Cohn admitted that such speculation on the appearance of life on earth went well beyond the limits of exact science; as long as we were aware of this fact, however, we might legitimately "fantasise" (28).

While Cohn used the problem of spontaneous generation as his starting point, Helmholtz arrived at the idea of the eternity of life from a cosmological perspective. In 1871, a few months before Sir William Thomson delivered his address in Edinburgh, Helmholtz gave a lecture, first in Heidelberg and then in Cologne, on the Kant-Laplace nebular hypothesis (29). To Helmholtz, this hypothesis of the origin of planetary systems was "one of the happiest ideas in science", which had proved to be of great heuristic value (30). After explaining the hypothesis, Helmholtz described how it implied that the physical conditions of the earth had changed, and will change, throughout its history and discussed the implications of these changes for life on earth. He argued that the first organisms on earth must have been adapted to the environment of the warm seas and could probably not have survived the cooler conditions we are used to now. Similarly, while we would regard a world without sun with horror, it was likely that new forms of life will evolve that could withstand the temperatures prevailing on earth as the sun is gradually extinguished. There would come a time, however, when life on earth will no longer be possible at all, but at such time other worlds might be ready to develop life. But how would life start on these other worlds?

Considering this question, Helmholtz noted that meteorites sometimes contain hydrocarbons and that the light of the heads of comets exhibit spectra resembling those of gases containing hydrogen and carbon. He continued,

> "But carbon is the element, which is characteristic of organic compounds, from which living bodies are built up. Who knows whether these bodies, which everywhere swarm through space, do not scatter germs of life wherever there is a new world, which has become capable of giving a dwelling place to organic bodies? And this life we might perhaps consider as allied to ours in its primitive germ, however different might be the form which it would assume in adapting itself to its new dwelling place." (31)

The final part of the lecture was taken up with a discussion of life as an imperishable, autonomous entity. Curiously, in view of the fact that the theory of cosmozoa was concerned with the space travel of material objects such as germs and spores and seemed to demand a fundamental dualism between living matter and non-living matter, Helmholtz suggested that the essence of life was an immaterial principle, implying a dualism between life and matter. He admitted that life had always been observed to be associated with organic matter, but suggested that it was not the substance constituting the body on which the continuance of the individual depends:

> "That which continues to exist as a particular individual is like the flame and the wave - only the form of motion which continually attracts fresh matter into its vortex and expels the old. The observer with a deaf ear only recognises the vibration of sound as long as it is visible and can be felt, bound up with heavy matter. Are our senses, in reference to life, like the deaf ear in this respect?" (32)

Before discussing Helmholtz's ideas on the nature of life further, brief mention should be made of another passage he wrote on the theory of cosmozoa, in the Preface to the German translation of Part 2 of the first volume of Thomson and Tait's Handbook of Theoretical Physics (33). Here Helmholtz answered a number of criticisms that had been made in Germany of the first part of the Handbook, including those of Zöllner mentioned above. He also took the opportunity of commenting on Zöllner's objections raised against Thomson's hypothesis of the appearance of life on earth, although this topic had not been treated in the Handbook. Pointing out that he himself had discussed views similar to those of Thomson slightly earlier in an, at that time unpublished, lecture, he could not understand Zöllner's objection that such ideas were unscientific. They were perhaps improbable, but not unscientific:

> "I cannot object if anyone considers this hypothesis to be in a high, or even in the highest, degree improbable. But it seems to me a perfectly correct scientific procedure that, when all our attempts to produce organisms from lifeless matter fail, we may enquire whether life has ever originated at all, whether it is not as old as matter itself, and whether its germs have not been transported from one world to another and developed themselves wherever they found a favourable soil." (34)*

Moreover, Zöllner's technical objections were of little weight: meteorites do get very hot when they enter a planet's atmosphere, but only on the surface, and any germs trapped in crevices inside meteorites would be safe.

Helmholtz, then, was confirmed in his conviction of the eternity of life. While Helmholtz did not discuss the wider implications of this view, his position appears strangely paradoxical: a physiologist who had waged one of the most influential battles against vitalism of his days here asserted the absolute autonomy of life. Together with Ernst Brücke, Emil Du Bois-Reymond and Karl Ludwig, Helmholtz had founded the "1847 school of physiology", which had as its aim to found physiology on the methods of physics and chemistry. According to this school of thought, any appeal to non-physical properties or forces in the explanation of biological processes was impermissible. Helmholtz himself had made a major contribution

*Ich kann nicht dagegen rechten, wenn Jemand diese Hypothese für unwahrscheinlich im höchsten oder allerhöchsten Grade halten will. Aber es erscheint mir ein volkommen richtiges wissenschaftliches Verfahren zu sein, wenn alle unsere Bemühungen scheitern, Organismen aus lebloser Substanz sich erzeugen zu lassen, das wir fragen, ob überhaupt das Leben je entstanden, ob es nicht eben so alt, wie die Materie sei, und ob nicht seine Keime von einem Weltkörper zum anderen herübergetragen sich überall entwickelt hatten, wo sie gunstigen Boden gefunden."

to the formulation of the law of conservation of energy and held that any postulates involving the action of a non-physical vital force constituted a breach of this fundamental law. Nevertheless, he suggested in his 1871 lecture that life might in fact be beyond our understanding, that it might be as sound is to the deaf ear. The clue to this apparent dichotomy may lie in the strong influence exerted on Helmholtz by Kant's epistemology.

In his Critique of Teleological Judgement, Kant argued that the physiological processes of living organisms can be understood in mechanistic terms, but that the origin and embryological development of organisms are beyond the human understanding, or transcendental (35). Organisms were self-organising beingsand were understood more readily in teleological than in mechanistic terms. In addition to its motive power, any organised being possessed an

> "...inherent formative power, and such, moreover, as it can impart to material devoid of it - material which it organises. This, therefore, is a self-propagating formative power, which cannot be explained by the capacity of movement alone, that is to say, by mechanism." (36)

Kant's critical teleology defined the limits of an empirical approach to biology. One of these limits concerned the impossibility of the artificial creation of living organisms: life could only come from life.

In a much more detailed analysis of critical teleology than the remarks made here, Nils Roll-Hansen has discussed the similarities between Kant's position and the scientific methodology of Claude Bernard (1813-1878) (37). While Bernard's "Physiological determinism" was founded on his belief in the value of the experimental methods of physics and chemistry for physiology, he accepted at the same time that there were absolute limits to the applicability of the experimental method in biology. In particular, an empirical approach to the problems of heredity and morphological development was impossible in principle; any explanation of these problems would require a subjective teleological principle (38). Granting the strong resemblance between the biological methodologies of Kant and Bernard, there was no direct historical link between the two. As pointed out by Roll-Hansen, Bernard only had a superficial knowledge of Kant's writings. The situation was different in the case of Helmholtz, who was deeply interested in and familiar with Kant's works, and the question arises whether Helmholtz might have favoured a similar methodology through the influence of Kant's writings on critical teleology.

At first sight, such an influence seems unlikely for two reasons. First, Everett Mendelsohn has argued that the ways in which physics and chemistry were incorporated in physiology in the mid-19th century differed radically in France and Germany (39). The French school of physiology, under the influence especially of Claude Bernard, introduced the experimental methods of chemistry and physics into biology but assumed that biology kept its special phenomena and its own laws. Some questions, such as that of the first cause of life, could not be explained in terms of physics and chemistry in principle. In Germany, on the other hand, a reductionist attitude prevailed; the explanatory models of the German physiologists were based on the assumption of the ultimate reducibility of all biological phenomena to the laws of physics and chemistry. Mendelsohn attributes the influence of this reductionist method to Theodor Schwann (1810-1882) and suggests that the latter inspired physiologists such as Helmholtz and Du Bois-Reymond to adopt a similar methodology.

Secondly, there is no clear evidence of an influence of Kant's critical teleology either in Helmholtz's own writings or in the secondary literature on Helmholtz. In fact, Helmholtz's attitude to Kant's philosophy was by no means an uncritical one and he did not accept Kant's ideas in toto. For example, while he accepted that the concept of space and the law of causality must be a priori, he could not agree that the axioms of geometry and the laws of mechanics could be derived from a priori principles (40). Moreover, Helmholtz acknowledged Darwin's contribution in showing that the purposiveness of living organisms might be the result of the action of natural laws without any intelligent intervention (41). Hence, there seems little room left for critical teleology.

Nevertheless, there is some evidence that the reductionism of the 1847 school of physiology, including that of Helmholtz, might be named more appropriately "critical reductionism". D.H. Galaty has presented evidence showing that the 1847 school based its arguments primarily on epistemology, rather than on scientific methodology (42). It was in the first instance the group's re-examination of such concepts as causal explanation, physical explanation and force, using reasoning derived from Kant, which led to the conclusion that there is only one kind of valid scientific explanation. The physiologists of the 1847 school therefore concluded that this explanation, in terms of attractive and repulsive forces, must be common to the physical and the biological sciences. However, their claim that physical phenomena and biological phenomena should be explained in the same terms did not, according to Galaty, entail that the phenomena studied by physical and chemical methods were <u>sufficient</u> to explain all organic function*.

Galaty particularly emphasises the strong influence of Kant on the 1847 school. Although the physiologists did not adopt all of Kant's arguments, they did adopt many, including Kant's central idea that there are limits to human knowledge. This idea was evident in Du Bois-Reymond's lectures on the limits to scientific knowledge and on the seven riddles of the universe (44). While Du Bois-Reymond did not regard the problem of the origin of life as a fundamental mystery, or a transcendental question, it is possible that Helmholtz did. Helmholtz accepted that there are limits to human understanding, believing, for example, that the nature of causality was a transcendental problem. Only the assumption that he regarded the question of the <u>origin</u> of life as a transcendental one is consistent both with his physiological reductionism and his statements on the eternity of life.

In this context, it is of interest that the neo-Kantian philosopher Friedrich Albert Lange (1828-1875) gave a

*In practice also the main influence of the 1847 group was due to the introduction of new methods of experimentation into physiology rather than to any success in reducing vital phenomena to chemistry and physics - which the members of the group did not in fact achieve (43).

sympathetic account of the theory of cosmozoa in The History of Materialism (45). He discussed the objection, which had been raised by many (46), that the assumption of an extraterrestrial origin of life did not solve the question of life's origin, but only pushed it further back: the world from which life on earth was derived must also have gone through a phase when it was glowing hot and incapable of harbouring life, so that this world in turn must have been seeded from another planet, and so on. Lange agreed that, on this view, the actual origin of life remained unintelligible, but added:

> "We find ourselves in a process ad infinitum, and this kind of 'postponement' has at least the advantage that it brings the unsolved difficulty into good company. The origin of life thus becomes as explicable and as inexplicable as the origin of the world generally; it comes into the sphere of transcendental problems, and to transfer it into this sphere is by no means logically improper, as soon as natural science has good grounds within its sphere of knowledge to regard such a theory of transmission as relatively the most probable." (47)

In the final analysis, however, Lange concluded that it would be premature to relax the experimental efforts to demonstrate a terrestrial origin of life from non-living matter, and that Ernst Haeckel's hypothesis in particular, however bold, ought to be explored further empirically.

A premature rejection of the possibility of a natural transition from non-living to living matter was also criticised scornfully by Friedrich Engels, who commented,

> "What Helmholtz says of the sterility of attempts to produce life artificially is pure childishness. Life is the existence of protein bodies....So long, however, as we know no more of the chemical composition of protein than we do at present, and therefore probably for another hundred years to come cannot think of its artificial preparation, it is ridiculour to complain that all our efforts, etc., have failed!" (48)

To Engels, life represented a stage in the general historical development of matter and he regarded the fundamental dualism between non-living and living matter implied by the theory of cosmozoa as particularly unpalatable. Ernst Haeckel also rejected the theory out of hand on the grounds of this "cosmological dualism" (49). Indeed, most of the contemporary criticism of the theory centred round this implication of the concept of the eternity of life. The implications were not clear to everyone, however. Max Verworn criticised the theory because it appeared to deny the possibility of any form of evolution whatsoever (50). Starting from the premiss that there is no fundamental difference between living and lifeless substance, he deduced that any theory dealing with the derivation of living matter must also be applicable to inorganic substance, Hence, he claimed, if it is assumed that complex compounds such as proteins have never originated on earth but have merely been transferred from another world, then we must assume that the same applies to complex inorganic compounds such as feldspar and quartz. The logical conclusion would be that all of the earth's compounds had wandered already complete into our planetary system from outside, a result which clearly contradicts our knowledge of physics, chemistry and geology. In conclusion, the theory of cosmozoa denied evolution, not only of living things, but of the whole earth itself.

There is an obvious flaw in Verworn's argument. His reductio ad absurdum is based on the premiss that there is no fundamental difference between living and non-living matter, which is precisely what the concept of the eternity of life, based on the impossibility of the generation of living from non-living matter, denies. In any case, the arguments raised against the theory of cosmozoa tended to be methodological and philosophical, rather than technical, ones. An obvious question which, besides the brief remarks of Cohn, was not raised concerned the problem how living organisms could survive the conditions of space for any length of time. The first serious attempt to fill this gap in the theory was not made until the beginning of the 20th century, by Svante Arrhenius.

Arrhenius: light, life and eternity

Besides his celebrated contributions to chemistry, Svante Arrhenius (1859-1927) published many books and articles of more general, especially cosmological, interest (51). One of his major concerns was with the question of the age of the universe, interpreted in the light of the first and second laws of thermodynamics (52). According to these laws, the energy of the universe is constant, while entropy tends to a maximum. The constancy of energy implied that the universe must be eternal - energy could not have been created out of nothing. However, if the universe had existed for eternity, maximum entropy would by now have been reached and all heat would have been dissipated. The latter conclusion obviously contradicted our experience and Arrhenius sought a way out of this paradox. The first law of thermodynamics was absolutely fundamental and could not be violated; he therefore asked whether any entropy-decreasing mechanisms were possible. The astronomically observed lack of uniformity of motion in the universe suggested to him that there might be local pockets in the universe where entropy was actually decreasing. With this solution of the paradox, the concept of the eternity of the universe became fundamental to Arrhenius' thought. He also applied the principle of eternity to the question of the origin of life.

In Worlds in the Making, Arrhenius presented a new version of the theory of cosmozoa, or, as he called it, panspermia (53). Starting from the evolutionary concept that all living beings on earth had ultimately descended from a single simple organism, he discussed previous attempts to account for the origin of this first organism. According to Arrhenius, the theory of spontaneous generation had been refuted decisively by the work of Pasteur, Tyndall and others. The hypothesis that some form of abiogenesis might have occurred at least once under special conditions was, he felt, without any experimental basis and misguided. He agreed with Sir William Thomson that this hypothesis was in conflict with philosophical uniformitarianism (although raising the statement that life always comes from life to the same status as the law of gravitation was "perhaps a little dogmatic"). The problem should be tackled in a radically new way, and such a way was provided by the theory of panspermia (54).

Arrhenius acknowledged Richter as the founder of the modern panspermic theory and agreed with the latter that the existence of life in the universe must be eternal. He commented,

> "Man used to speculate on the origin of matter, but gave that up when experience taught him that matter is indestructible and can only be transformed. For similar reasons we never inquire into the origin of

> the energy of motion. And we may become accustomed to the idea that life is eternal, and hence that it is useless to inquire into its origin." (55)*

Arrhenius could not, however, accept the technical details of Richter's hypothesis and thought that a transfer of germs by meteorites was highly unlikely. Apart from the fact that there was no evidence for the organic origin of carbon found in meteorites, the surface of these bodies becomes far too hot during their flight to allow the survival of any organisms they might carry. Richter's idea that germs floating high in the atmosphere might be picked up by passing meteorites was said to be "still more fantastic" (56). Thomson's hypothesis suffered similar defects. The violent impact of the collision between large celestial bodies would generate enormous amounts of heat due to friction, which no living organisms could possibly survive. Besides, Arrhenius thought that such collisions were extremely rare events in the universe.

The matter did not rest here, however. A fresh approach to the problem had become possible now that the pressure exerted by solar radiation had become better understood, thanks to Maxwell's theory and Lebedev's experiments. It had been calculated that bodies of a diameter of 0.00016 mm were subject to the strongest influence of solar radiation and bacterial spores of such size were known to exist. Hence,

> "It is, therefore, very probable that there are organisms so small that the radiation pressure of a sun would push them out into space, where they might give rise to life on planets, provided they met with favorable conditions for their development." (57)

*Arrhenius appears to imply here that there may be a "law of conservation of life" at work in nature.

Taking the specific gravity of such an organism to be roughly the same as that of water, and assuming that the solar radiation pressure was approximately four times as strong as the effect of gravity, Arrhenius calculated that a terrestrial spore could undertake the following journey: the spore would cross the orbit of Mars in 20 days, that of Jupiter after 80 days, and that of Neptune after 14 months. The nearest solar system, Alpha Centauri, would be reached in 9000 years.

But would the germinating power of spores be retained during the entire course of such a journey? At the beginning of their travels, the spores would be exposed to intense solar radiation for about one month, and it had been shown that bacteria and their spores are readily killed by the most refrangible (ultraviolet) rays of the sun. However, Arrhenius questioned whether this lethal effect was due to the radiation itself. In Paris, Emile Roux (1853-1933) had shown that anthrax spores, which are normally killed by light, could be irradiated with impunity providing that air was excluded from the containers; some spores, for instance those of <u>Thyrothrix scaber</u>, withstood irradiation with sunlight for as much as a month in the absence of air. Arrhenius therefore concluded that the destructive effect of light on bacteria and their spores was due to some oxidative process mediated by the surrounding air. In space the spores would be in a vacuum, so that this oxidative process could not exert its lethal effect (58).

The next problem would arise once the spores had passed the orbit of Neptune; would they be able to survive the extremely low temperatures of -222°C and less, encountered further out in space? In answer to this question, Arrhenius cited experiments performed at the Jenner Institute in London in which bacteria were kept at -252°C in liquid hydrogen for 20 hours without losing their germinating power. It had also been shown that bacteria kept in liquid air at -200°C for 6 months retained their germinative capacity. Presumably, wrote Arrhenius, the loss of germinating power must be due to some chemical process and as all chemical processes are slowed down at lower temperatures, the germinating powers of organisms would in fact be retained longer under conditions of extreme cold. Vital reactions had been shown to be intensified by a factor of 2.5 when the temperature is raised by 10°C. From this, Arrhenius calculated that the germinating power of spores at -222°C would diminish no more over a period of $3 \times 10^6$ years than it would during one day at 10°C. It was reasonable to assume, therefore, that the intense cold of spacewould act as a preservative on the spores (59). Similarly, the absolute dryness of space would have a preservative effect.

One problem remained, namely how the spores could escape from the earth against the effects of gravitation in the first place. Here, too, an answer could be provided. Upward air currents might easily sweep spores up to a height of 100 km. At that height, there were always electric discharges, as indicated for example by the phenomenon of radiating aurorae, which would be strong enough to push particles up against gravity. The required field strength was as low as 200 V/m, which was near-normal and would certainly be exceeded in regions where there was an auroral display. Hence,

> "It is thus probable that germs of the lowest organisms known to us are continually being carried away from the earth and the other planets upon which they exist. As seeds in general, so most of these spores, thus carried away, will no doubt meet death in the cold infinite space of the universe. Yet a small number of spores will fall on some other world, and may there be able to spread life if the conditions be suitable." (60)

In order to escape the radiation pressure of the sun in another solar system, the spores would have to become attached to grains of interstellar dust, large quantities of which were known to exist. The higher density of the grains would ensure that the effect of gravitational forces pulling the particle down to a planet would exceed the pressure of solar radiation. In this way, life might have been transplanted from solar system to solar system since time immemorial. Finally, all organic beings in the universe should be related to one another on this theory - they should all consist of cells built up from carbon, hydrogen, oxygen and nitrogen. After emphasising the "perfect consistency" of his theory, Arrhenius ended on a cautious note:

> "There is little probability, though, of our ever being able to demonstrate the correctness of this view by an examination of seeds falling down upon our earth." (61)

Only a few spores derived from other worlds could be expected to fall on earth every year and, moreover, such spores would resemble terrestrial spores that had been picked up by the wind and then dropped on earth again. Hence it would be difficult, if not impossible, to prove the celestial origin of any spores encountered on earth.

Arrhenius' final comments highlight the problem of the testability of the theories of cosmozoa and panspermia. The claim that, millions of years ago, life on earth evolved from a seed or spore derived from another planet is not testable in principle. However, supporting evidence for the claim might be provided if it could be demonstrated that living seeds still reach the earth from outer space. But, according to Arrhenius, we would not be able to distinguish between extraterrestrial and terrestrial spores, so that this avenue was also closed. Arrhenius changed his mind on this latter point, however. In his last article, published posthumously in 1927, he claimed that the existence of thermophilic bacteria on earth provided proof for the panspermic hypothesis (62). Thermophilic bacteria, which had been discovered in the late 1880s, could only grow at temperatures between 40°C and 80°C or higher. Therefore, argued Arrhenius, the origin of a thermophilic branch of bacteria could only be explained by the assumption of long periods when the environmental temperature was between 40 and 80°C, during which the gradual process of adaptation took place. The earth did not nowadays provide such an environment, so it was likely that these bacteria were reaching the earth continuously from a warmer planet. The most likely candidate was Venus, which had a surface temperature of 50°C and was periodically positioned between the earth and the sun, so that the journey would only take a few days. Conditions on earth were not such that thermophilic bacteria could survive from year to year, so that a continuous supply from another planet was required.

In this respect, Venus seemed the obvious source. The thermophilic bacteria therefore provided empirical proof ("ein experimenteller Beweis") for the transfer of germs from Venus to the earth by the pressure of solar radiation (63).

Arrhenius' argument reflects a gross misunderstanding of the concept of adaptation, especially with respect to microbes. Bacteria are not adapted to the general environment, but to specific habitats presenting a wide range of conditions. Thermophilic bacteria are adapted to the environment of hot springs, cryophilic bacteria are adapted to cold conditions, anaerobic bacteria live in the absence of air, and so on. Why should thermophilic bacteria not have evolved in hot springs and survive in the same habitat from year to year?

In the meantime, however, Arrhenius' theory had been tested on some of its technical claims. Paul Becquerel was interested in the specific claims made by Arrhenius regarding the viability of bacteria and their spores in the conditions of space (64). He and his colleagues confirmed, in experiments performed in the cryogenic laboratory of Kamerlingh Onnes in Leiden, that bacteria and their spores survive extreme cold over long periods. In fact, bacteria retained their germinating power for as long as two years when kept at very low temperatures *in vacuo* (65). However, Becquerel also showed that ultraviolet irradiation does kill bacterial spores even when air is excluded. In the experiments of Roux, the spores were protected from this effect because Roux used glass tubes and the glass absorbed the ultraviolet rays. Becquerel repeated the experiments using a quartz plate and, because quartz lets through ultraviolet rays, all spores were killed. This had nothing to do with oxidation processes; the lethal effect was entirely due to the radiation (66). Moreover, in space the spores would be exposed to even worse hazards, such as X-rays and $\gamma$-rays. With so many dangers, the hypothesis of Arrhenius crumbled.

Indeed, the panspermic hypothesis soon lost its support although it continues to be revived in different form from time to time, sometimes only half-seriously, and still seems to have much appeal to the imagination*. Before discussing these later trends, however, a few remarks must be made about the foundations of Arrhenius' theory of panspermia. In a study of this question, Dick Haglund has reached the conclusion thatthere was no strong religious influence on Arrhenius, no argument of design, and no specific metaphysical influence (67). It was on scientific theoretical grounds that he reached the conclusion that the universe was infinite; he showed no great interest in the epistemological consequences of such a view. He accepted limits to scientific knowledge: we did not enquire into the origin of matter or of energy - and he was prepared to place the question of the origin of life in the same domain. He did not justify his claim of the eternity of life, nor did he discuss its consequence of the absolute autonomy of life. The theory of panspermia simply provided a consistent picture with his cosmological theories in general. While the latter may have been

*As witnessed, for example, by the publicity given in the press, on the radio and television to Fred Hoyle's recent version of the theory (see below).

based soundly on theoretical physics, chemistry and astronomy, it cannot be said that his theory of panspermia was soundly based on biological theory.

As has been mentioned above, Arrhenius' paper on thermophilic bacteria revealed a misunderstanding of the concept of biological adaptation: thermophilic bacteria could not have evolved on earth because they were not adapted to the present (general) environment of the earth. This suggests that Arrhenius was among those who rejected a theory of chemical evolution and abiogenesis under special conditions on the grounds that the conditions which sustain life today must have been very similar to those under which life arose (68). On this argument, a hypothesis which depended on "special conditions" was unacceptable. But Darwin had already shown an awareness of the fact that the most important feature of these special conditions is that a prolonged chemical evolution was only possible under sterile conditions*, and it was an accepted fact that the earth had once been lifeless. Moreover, the organic molecules formed by a process of chemical evolution would be best protected from destruction by oxidation in an atmosphere without free oxygen. In fact, Arrhenius did think that the original atmosphere of the earth was without oxygen (70). Nevertheless, he believed that small amounts of oxygen must have been available (for example from the dissociation of carbon dioxide) by the time life

*Darwin's statement on this question was included as a footnote in The Life and Letters of Charles Darwin, published in 1887 (69). Its significance does not seem to have been grasped by his contemporaries.

started on earth, because oxygen was indispensible for life. (In the same book, he later suggested that anaerobic bacteria were degenerate plants (71).) He never discussed these points in relation to the problem of abiogenesis, however, and it appears that Arrhenius never considered a terrestrial origin of life from inorganic matter very seriously. His understanding of biology was not deep and the theory of panspermia made it possible for him to treat the problem of the appearance of life on earth primarily as a physical problem and, moreover, to bring it in line with his treasured concept of the infinity of the universe.

Modern panspermia - fact or fiction?

The idea that living matter is eternal, which would imply that complex organic compounds such as proteins and nucleic acids have always existed in the universe, is no longer consistent with modern cosmogenic theories. In addition, few biologists would now accept that the question of the origin of life is beyond the limits of scientific knowledge. It is not, however, necessary to adopt the philosophy of the eternity of life in order to entertain the view that life on earth is ultimately derived from elsewhere in the universe. In a general discussion of panspermia, Leslie Orgel points out that there is no compelling reason to reject the possibility that the first cell on earth arrived within a meteorite, where it would be protected from extreme temperatures and lethal radiation (72). Apart from the fact that careful investigation has never yet shown the presence of carbon compounds of biological origin in meteorites, however, the theory does not in fact offer many advantages: the additional freedom gained in choosing from a wider range of possible prebiotic environments is not very helpful:

> "The conditions that we customarily assume to have existed on the primitive earth are as favorable for the origin of life as any that can be reasonably postulated for any other planet." (73)

But the hypothesis may have other advantages. It might, for example, provide an explanation for the universality of the genetic code of terrestrial organisms. If life on some other planet exhibited greater diversity in its genetic material, and if one organism from this planet, with the basic genetic make-up now encountered on earth, had been carried to earth, one of the most difficult problems concerning the origin of life would be solved*. In addition, the use made by living organisms of the trace element molybdenum instead of the more abundant, chemically similar element chromium led Orgel, together with Francis Crick, to suggest that life had reached the earth in the form of an organism derived from a molybdenum-rich environment elsewhere in the universe (75)**. However, it has been argued recently, on the basis of a geochemical model, that molybdenum is leached from rocks more effectively than chromium, so that its

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*Two Soviet theoreticians have argued, on the basis of a rather complex mathematical model, that the coexistence of more than one genetic code would inevitably lead to an unstable situation and to the elimination of all but one (74). If this is correct, the molecular biology of primitive life on earth may have been more varied and its present universality may be a product of a "struggle for existence".

**Crick and Orgel speculated that life might have been brought to the earth in an alien space craft. Carl Sagan recounts that a related suggestion was made by Thomas Gold of Cornell University. Gold envisaged alien visitors having a picnic on the virgin planet and leaving their refuse behind, resulting in microbial contamination. Sagan calls this the "garbage theory of the origin of life" (76).

concentration in sea water is correspondingly higher (77). The same model suggests that the relative concentrations of the two elements in sea water would have been established early in the history of the oceans, so that the use of molybdenum by organisms in preference to chromium is consistent with the hypothesis of the gradual evolution of life in the primaeval oceans. This example illustrates the pitfalls of giving up one's hypotheses too readily. However, Crick and Orgel made their suggestion of an extraterrestrial origin of life only half-seriously and certainly have not given up trying to account for the terrestrial origin of life in general and of the genetic code in particular. A more seriously intended hypothesis of panspermia has been proposed in recent years by the astronomer Sir Fred Hoyle.

The panspermic hypothesis of Hoyle and his co-worker Chandra Wickramasinghe is the outcome of a series of investigations of absorption spectra of interstellar dust and grain clumps. While the reports of these investigations (78) include only brief and, as the authors admit, speculative remarks on the question of the origin of life on earth, they have subsequently published a book concerned entirely with this question (79). The major claims made in this book are the following: firstly, within interstellar gas clouds a wide range of complex organic molecules are formed, particularly polysaccharides and "nitrogenated ring molecules", resembling porphyrins. Secondly, these "biomolecules" provide the building blocks for the emergence of more complex moieties which eventually develop into living cells. Thirdly, the earth was a possible site for the fitting together of biomolecules into the more complex forms, but appears less favourable than a site of comet-type bodies.

The evidence presented for the first claim is given in a resumé of the results published previously in Nature (see ref. 78)*. The infrared emission spectra of a wide range of galactic sources, and especially interstellar grain clumps, exhibit strong absorption at the wavelengths of 3 μm and 8-12 μm, as well as a feature at 18 μm. These spectral characteristics agree closely with the calculated spectrum of cellulose. In fact, the closest fit of a wide range of observed astronomical infrared sources is obtained with "an ensemble of polysaccharides", with an admixutre of simple hydrocarbons. Hence, polysaccharides with some hydrocarbons are present in large quantities within interstellar clouds (80).

This "evidence" has been subjected to a severe critique by Sagan and Khare (81). Firstly, they point out that the 3 μm absorption corresponds to the characteristic vibrational transitions of O-H, N-H and, particularly, C-H bonds while the 8-12 μm region is characteristic of C-C, C-O and C-N groups. Hence, there is considerable room for freedom in the interpretation of the spectra considered by Hoyle**. Secondly, polysaccharides only contain H, C and O and do not reflect the high cosmic abundance of nitrogen and sulphur. Sagan and Khare themselves favour an interpretation of the spectra in terms of

*Lifecloud does not include a reference list or a bibliography, nor are specific references cited in the text.

**The uncertainty of the interpretation of the spectra has also been mentioned in reviews of the book (82).

mixtures of substances ("tholins") which do reflect this abundance. Thirdly, there is no such thing as a common infrared spectrum of all galactic sources. The very variability of infrared spectra from source to source would suggest that a large variety of molecules, rather than a single class such as polysaccharides, are responsible. Finally, no plausible mechanism for the formation of polysaccharides in the interstellar medium has been presented, nor is such a mechanism easily envisaged. All that can be added to these comments is that an exhaustive list of interstellar molecules, recently published in Nature (83), does not include polysaccharides, nor the bicyclic nitrogen compounds, of Hoyle and his co-author*.

The second claim of Lifecloud is not backed up with evidence at all - it is merely suggested that many complex organic molecules may exist in gaseous form so close to the nuclei of comets that they are difficult to detect. It is also suggested that the small molecular species that have been detected in comets are dissociation products of organic polymers such as polysaccharides (84).

The third claim is supported with four major arguments, to which a fifth one has been added since the book was written. First of all, Hoyle and Wickramasinghe claim that there is no evidence that the primaeval atmosphere of the earth was a

*Presumably this omission indicates that the compilers of the list also disagree with the interpretation of the spectra favoured by Hoyle and his colleagues.

reducing one, as demanded by the Oparin-Haldane hypothesis*. With an oxidising atmosphere, the processes envisaged by this hypothesis would be seriously disrupted, thus making the earth an unlikely candidate for a site of chemical evolution. In fact, there is evidence that the primaeval earth's atmosphere was a reducing one. Petrological studies have shown that large amounts of ferrous iron were deposited in Precambrian times while all younger rocks contain iron in the oxidised, ferric, form (85). These and other geological data indicate that the early Precambrian atmosphere was a reducing one. In addition, the composition of the atmospheres of the planets in the solar system reflects the dominance of hydrogen in stellar material and in the cosmos in general (86). The earth would, therefore, be exceptional if its primaeval atmosphere were an oxidising one. The present oxygen content of the earth's atmosphere can be accounted for primarily by $O_2$ derived from plant photosynthesis and, to a lesser extent, the photodissociation of carbon dioxide (most of which is produced by respiring organisms).

Secondly, Hoyle and Wickramasinghe argue that all volatiles in the earth's atmosphere probably came from outside comparatively late in geological history, together with the complex biochemicals required for the origin of primitive life forms** (87). However, the vast range of abiogenic syntheses performed

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*See Chapter VII of this thesis.

**In the introductory chapters it is stated: "If the earth is being showered with precisely the right biochemicals for life, *as we know it to be*, why choose the more complicated explanation?" (88). (my italics - HK) under simulated prebiotic conditions indicate that a great variety of "biomolecules" are formed under a wide range of conditions and using different sources of energy (such as electrical discharges, ultraviolet radiation and heat). Hence, there is no need for the hypothesis that "biomolecules" arrived on earth from outer space, especially as the interstellar medium would seem to provide a more hostile environment than the primitive earth.

Thirdly, the authors argue that, not only "biomolecules", but life itself may have reached the earth from outer space. This assumption would make it easier to understand the chemical and biochemical uniformity of terrestrial organisms (89). On this point, Sagan and Khare comment that there seems to be no way for organisms to evolve in the interstellar medium: conditions are such that organic reaction rates would be negligible (90). In addition, in an extremely detailed study of the chemistry and biochemistry of organisms in relation to the chemistry of the terrestrial environment, A.E. Needham shows how organisms have successfully exploited the materials available in this environment (91).

Fourthly, Hoyle and Wickramasinghe claim that Darwinian evolution by natural selection alone fails to account for the vast elaboration of species evidenced in the palaeontological record and that the required increase in genetic information may well have resulted from "continuing viral invasions from outside" (92). Later the authors added a new twist to this argument: the sudden incidence of viral epidemics (sometimes in widely separated places at the same time) and their variable effects on different individuals in the same place is to be explained readily on the hypothesis that new viruses repeatedly arrive on earth from outer space (93). Several comments may be made here. All known viruses have a molecular biology typical of indigenous terrestrial organisms, and the stochastic nature of the evolutionary process makes it highly unlikely that the biochemistry of all extraterrestrial organisms would resemble that of indigenous organisms so closely. In addition, the typing of viruses over several decades has shown that the influenza virus, among others, has changed only slightly over the course of several epidemics separated in time. These changes are readily explained on a hypothesis of random mutation, whereas a panspermic theory would have to assume that viral invasions from the same galactic source had occurred at separate times. Finally, in the transmission of viruses we have to take into account, not only transmission from human to human in a particular region, but also transmission by (possibly migrating) animals and between widely separated regions by modern means of transport such as aeroplanes (94). Much could be added, but the above comments should serve to illustrate that Lifecloud presents an over-speculative theory based on ill-founded arguments, including many factual errors*, and provides no great recommendation for the concept of panspermia.

*To name a few examples, in their explanation of molecular asymmetry, the authors use as an example the amino acid glycine, which is the only common amino acid that does not have an asymmetric carbon atom. Instead of the usual terms heterotrophic and autotrophic organisms (denoting the capacity to feed only on organic matter and on inorganic matter, respectively) the authors use the terms heterotropic and autotropic. Finally, the structure of chlorophyll, given on page 51, includes several errors.

In conclusion, then, the concept of the eternity of life that was at the root of earlier panspermic theories led to philosophical problems with respect to the idea of the absolute autonomy of life and the epistemological limits it imposed. Panspermic theories which dispense with the idea of the eternity of life, however, so far have not offered any advantages over the hypothesis of a terrestrial origin of life from non-living matter. Many difficult problems remain, as will be shown in the final chapter of this thesis, but the idea of panspermia does not solve them.

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## Chapter IV
## SPONTANEOUS DEGENERATION: THE LIVING ORIGINS OF INORGANIC MATTER

The idea that life had existed for eternity was incorporated in another 19th-century hypothesis on the origin of life which is discussed in a number of reviews (1). According to this hypothesis, life in the universe not only had no beginning but actually preceded the formation of the inorganic world. This curious theory had no lasting influence, but it supports the view that the problem of the origin of life had reached a crisis and a brief discussion of its contents and foundations is therefore warranted. The hypothesis was given its most explicit formulation by William Thierry Preyer (1841-1897) but the central idea had been presented slightly earlier by Gustav Theodor Fechner (1801-1887), whose views will therefore be discussed first.

### Fechner's "cold death" of the universe

Gustav Fechner obtained a medical degree at the University of Leipzig but, instead of practising medicine, embarked on research in chemistry and physics (2). In 1834 he was appointed Professor of Physics at Leipzig, a position from which he had to resign in 1839 because of a serious neurotic illness. Upon his recovery, he started a scientific investigation of the relations between mind and body, in particular the relations between sensation and external stimuli. Thus he became the founder of "Psychophysik", or sense physiology, a field in which Preyer also was to become active. Fechner's interests ranged widely; he founded a branch of knowledge called "experimental aesthetics" and, in 1873, published his unorthodox views on the origin of life under the title of Einige Ideen zur Schöpfungs- und Entwickelungsgeschichte der Organismen (Some ideas on the origin and evolution of organisms) (3).

In this little known monograph*, Fechner proposed that, instead of using chemical criteria, a state of molecular motion ("moleculare Bewegungszustande") be adopted as the fundamental characteristic of the organic world. Although he denied that there was a fixed borderline between the organic and the inorganic, Fechner believed that a relative distinction could be made based on the state of motion of the particles making up the molecules of the respective domains: inorganic molecules can only change the position ("Ort") of their constituent particles while organic molecules can change spontaneously both the position and the arrangement ("Ort und Ordnung") of their elements (4).

Fechner claimed that all vital phenomena could be explained using this criterion. Moreover, it could explain the transition from the organic to the inorganic state that was characteristic of death** - precisely the point where a chemical criterion failed. To quote Fechner's example:

> "...upon boiling, an egg can, without any change in its complex chemical composition, pass from the organic to the inorganic state, in so far as we have characterised the latter by the lack of those vital phenomena or ability to develop that are exhibited by the organic state" (5)***

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*Of the reviews cited under ref. 1, only Lippmann's includes a mention of Fechner's work. Fechner's book is not cited in the entry on Fechner in the Dictionary of Scientific Biography.

**It should be noted that Fechner equated the organic with the living and the inorganic with the non-living. Accordingly, he regarded anything that is not actually alive as inorganic, regardless of its chemistry and regardless of its history.

***"...ein Ei kann durch kochen ohne Veränderung seiner complexen chemischen Constitution aus dem organischen in unorganischen Zustand übergehen, sofern wir diesen durch den Mangel der Lebenserscheinungen oder Entwickelungsfähigkeit, (cont. next page)

In addition to his criterion of molecular motion, Fechner introduced a principle that he considered to be absolutely fundamental, the principle of the tendency towards stability ("das Prinzip der Tendenz zur Stabilität")*. Equating instability with highly irregular movement and stability with regular, periodic movement, Fechner declared organic matter to be clearly less stable than inorganic matter. Any hypothesis based on the assumption that the organic world is derived from inorganic nature would therefore contradict the principle of the tendency towards stability. On the other hand, the transition into the inorganic condition which all organisms undergo, namely when they die, was in strict accordance with the principle (6). Hence Fechner rejected the "traditional view" according to which the organic world was generated in primaeval times from inorganic matter and a simple cell was produced at least once. Instead, he proposed the opposite view, namely that the inorganic world was ultimately derived from the organic domain. This hypothesis was not only consistent with the principle of the tendency towards stability but was also in accordance with observation: while the inorganic world had never yet shown itself capable of bringing forth the organic, it was observed daily that inorganic substances are excreted or deposited internally by living organisms (7).

(Footnote cont.) welche der organische Zustand darbietet, charakterisiert haben". By modern chemical criteria, the profound intra- and intermolecular changes involved in the denaturation of proteins (such as occur upon boiling) would be sufficient to explain a transition from the living to the non-living state.

*This principle is of course in direct contradiction with the second law of thermodynamics. The importance that was soon to be attributed to the latter presumably accounts for the lack of popularity of Fechner's principle.

The history of living organisms as we know them was then placed in the wider context of the history of life as a form of molecular motion. According to Fechner, the earth had passed through three different phases: a cosmo-organic ("kosmorganisch"), a molecular-organic ("molecularorganisch") and a molecular-inorganic ("molecularunorganisch") phase. During the first phase, the elements had not yet organised themselves into molecules and the earth was just a whirling mass of gases. At this stage, the cosmos itself was alive. Subsequently, the earth evolved into a solid mass in which particles continuously changed their position and relative arrangement. At that, molecular-organic, stagethe earth was a single giant organism (by Fechner's criterion of molecular motion), not yet mixed with inorganic matter. Finally, as the mass of the planet became more dense, a differentiation between organic and inorganic matter took place and the earth entered its present molecular-inorganic phase (8).

Although current theories of descent only covered a limited span of the history of life as Fechner defined it, he felt that the theory of evolution was consistent with his scheme: the evolution of living organisms in the traditional sense had led to ever greater stability. At the same time, he was led to the dubious conclusion, that, according to the principle of the tendency towards stability, life must have been more abundant on earth in the distant past than it is now (9). However, Fechner would probably not have been impressed with palaeontological evidence to the contrary because his criterion of life encompassed so much more than what most biologists would regard as living organisms.

If the earth itself was alive in the past, why worry about the absence of fossils in old rocks?

As for the future, which was not discussed by Fechner, the outlook for evolution seems bleak: according to the principle of the tendency towards stability, life must necessarily be extinguished, not as a result of environmental catastrophes or other external influences, but because of the inherent properties of matter. In Fechner's scheme, the "survival of the fittest" ultimately meant the "survival of the deadest".

Protoplasm: the vital remains of a dying planet

Fechner's speculations had little lasting influence but he made at least one immediate convert, namely William Preyer. Between 1873 and 1874 Fechner and Preyer wrote to each other extensively about scientific matters of mutual interest, mostly on vision, hearing and other areas of "Psychophysik" (10). In a letter written on the 2nd of January, 1874, Preyer referred to Einige Ideen zur Schöpfungs- und Entwickelungsgeschichte der Organismen (ref.3) and wrote that already on first reading he was completely convinced of the enormous significance of the basic idea of the book. He only expressed his regret that the theory as a whole was presented in rather embryonic form. Brief references to the book were made in four other letters exchanged by the two men during the first half of 1874, but after that the topic disappeared from the correspondence. Preyer's adaptation of Fechner's theory, which will be discussed below, does not appear to have been mentioned in the correspondence at all*.

*There are, however, two large gaps in the collected correspondence; there are no letters dated between July 1874 and September 1877, nor between October 1877 and November 1882. Preyer, who edited the collection, did not explain whether (cont. next page)

William Preyer was born in England and emigrated to Germany during his school days (11). He studied physiology and chemistry at the University of Heidelberg where he received his doctorate in 1862. After that he turned to medicine and studied first in Paris with Claude Bernard, then in Berlin, Vienna and Bonn. He obtained his medical degree in 1866, and from 1869 until 1888 held the Professorship of Medicine at the University of Jena. His research work was in the fields of physiological chemistry, sense physiology and psychology, his most famous contribution being the work Die Seele des Kindes, published in 1882. In addition, he was interested in more general scientific subjects such as the problem of the origin of life.

In 1873, Preyer published a booklet entitled Über die Erforschung des Lebens (On the investigation of life) (12), which is based on a lecture delivered in Leipsig to the "Versammlung deutscher Naturforscher und Aerzte" in August, 1872. In this treatise Preyer expressed his belief that not all phenomena of life could be explained on a mechanistic basis, in particular consciousness and other psychological phenomena. Why this should be so was not immediately apparent from an examination of the general conditions of life (oxygen in the air, water, a number of chemical elements, and warmth or light). However, one of the elements necessary for life was unique according to Preyer and this element, carbon, might play a special role in living organisms. The position of carbon was

(footnote cont.) no letters were exchanged between Fechner and himself during these periods or whether letters were written but for some reason not included in the published correspondence.

unique in that all carbon on earth appeared to be derived from living organisms; even graphite and diamonds were of organic origin, being the remnants of vegetable matter. Also the carbon dioxide in the environment was mostly a product of the combustion of organic matter, although Preyer admitted that some carbon dioxide was exhaled by volcanoes. The latter process, however, could only release small quantities of $CO_2$ into the atmosphere, by no means sufficient to serve as a carbon source for the generation of living organisms. The unique position of carbon therefore posed a problem: if it were true that carbon was an element in the chemical sense, that is, undivisible, unchangeable, without origin and indestructible, then it became incomprehensible that carbon was nearly always found as a constituent or product of living organisms. If the latter actually gave rise to carbon, then it could no longer be strictly regarded as an element. Preyer continued,

> "I here merely wish to bring to your attention the difficulty, which is greater than appears to have been assumed so far and forces us to question the elementary nature of carbon. As long as this problem remains unsolved, there can be no question of the 'How?' of the first origin of life on earth." (13)*

Preyer made no attempt to overcome the difficulty of the origin of carbon at this stage and let the matter rest here. A few years later, however, he presented a hypothesis on the origin of life which took the problem into account and which

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*"Ich will hier nur auf die Schwierigkeit aufmerksam machen, welche grosser ist, als man bisher angenommen zu haben scheint und stark an der elementaren Natur des Kohlenstoffs zu zweifeln zwingt. So lange diese Frage nicht erledigt ist, kann von dem Wie? der ersten Entstehung des Lebens auf der Erde nicht die Rede sein."

also incorporated some of Fechner's ideas (although the latter were not acknowledged as being due to Fechner). Preyer's hypothesis was first published in 1875 and subsequently included in a collection of his papers (14).

Preyer started by commenting in detail on the two main rival hypotheses on the origin of life, the abiogenesist or evolutionary position and Richter's theory of cosmozoa. He pointed out that the acceptedview that the earth's surface had once been too hot to support life usually led scientists to the conclusion that life on earth must have had a definite origin in time. According to one view, organisms resembling the most primitive living beings known today had arisen at least once from non-living matter. As there was no evidence to suggest that such a process could take place on earth today, the proponents of this view were forced to claim that the conditions on earth at the time when its surface was cooling down were very different from those encountered today. Thus, it was under unique conditions that the unique process leading to the origin of life took place until the conditions changed so much that living organisms could no longer be generated except from other organisms. But life was sustained under a rather limited range of conditions and Preyer doubted that any organisms living under radically different conditions could have survived at all (15).

Preyer was rightly dissatisfied withthe postulation of a unique, but undefined, process taking place under unique, but undefined conditions. Rather than demand that a serious attempt be made to provide the missing details and to explain in concrete terms why the Urzeugung no longer appears to take place on earth now, Preyer took another course:

> "Such a view is so unsatisfactory that I prefer to ask: Could the Urzeugung on our planet be altogether impossible - once, now and forever?" (16)*

Preyer also presented a logical argument for questioning whether life could ever have arisen on earth from inorganic matter. It was a general observation that living things appear only where there was life before. Similarly, experience taught that all organisms die eventually. While no one doubted that all that lives will die, however, there did not seem to be similar agreement on the equivalent inductive generalisation that life must always come from life. But if experience was good enough proof for the former, it should be good enough proof for the latter, the two statements being entirely equivalent ("volkommen gleichwertig"). Admittedly, neither statement had been proved deductively, but the inductive proof had at least made the possibility of an Urzeugung highly improbable:

> "Anyone who looks for an organism that has not been born, but came into being by means of an Urzeugung, i.e. was built up from dead corpuscles, has even less prospect of finding it than someone who looks for an organism that cannot die." (17)**

This conclusion was based on purely quantitative grounds: we knew that all organisms alive today had been born while each of us had only been confronted with a limited number of deaths. It must be said that the Urzeugung is automatically excluded on

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*"Eine solche Auffassung ist so unbefriedigend, dass ich vielmehr frage: Sollte die Urzeugung auf unserem Planeten überhaupt - einst, jetzt und künftig - unmöglich sein?"

**"Wer nach einem Organismus sucht, welcher nicht geboren wäre, sondern dürch Urzeugung entstanden, d.h. aus todten Körpern zusammengefasetzt, hat noch weniger Ansicht zu finden, als Einer, welcher nach einem Organismus sucht, der nicht sterben könnte."

logical grounds only if the two inductive generalisations that "all organisms are born" and that "all organisms will die" are regarded as symmetrical. If the generalisations include statements about the past (for instance that all living organisms have always been born from other living organisms) then the main question is precisely whether they are factually equivalent and not how many instances can be provided in their support from the present.

Preyer was more sympathetic towards the theory of cosmozoa as formulated by Richter. He did not envisage any technical difficulties for its auxiliary hypotheses. First, the fact that spores on earth could remain dormant for long periods, and under adverse conditions, without losing their germinating power supported the possibility that the cosmozoa could retain the capacity to live in the hostile surroundings of space. Secondly, there was no evidence to contradict the requirement that germs similar to those on earth existed on other planets. Thirdly, while Richter's proposal that germs float through space independently posed certain difficulties, it was not essential to the central idea of the theory and could be replaced by the suggestion that the germs were attached to and protected by meteorites. With such a mechanism the germs could retain their viability during their journey through the atmosphere of the earth or other planets.

Technically, therefore, the theory was worthy of consideration - only the presence of germs in meteorites remained to be demonstrated. Nevertheless, it was still necessary to answer the question of how the germs that populated the earth from space had come into being in the first place. Either the germs arose from inorganic matter on some planet somewhere in the universe or protoplasmic germs had always existed, throughout eternity. In the first case we were back to the unsatisfactory problem of the Urzeugung - it had merely been transposed from earth to another planet. The second possibility, which was in fact proposed by Richter, implied that protoplasmic germs, or even whole plants that yielded seeds, were as old or older than the sun itself (18). Preyer regarded the latter view as highly implausible although he failed to explain why*. He therefore felt that a radically new approach to the problem was needed. We should reverse the question and ask

> "...whether perhaps the unorganised dead bodies arose from organised living things ..." (19)**

To deal with this question, Preyer first referred to his previous argument that all carbon on earth is derived from living organisms. Hence, there was no reason to believe that any carbon existed on earth before it was inhabited by life. It was much more likely that vital processes preceded the formation of the earth and gave rise to all inorganic things as products of excretion, solidification, decay and cooling (20).

Preyer next considered the criteria that were used to distinguish between the living and the non-living and concluded that the only distinguishing feature that was applicable consistently

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*It is possible that Preyer felt there was a contradiction between an evolutionary view of planetary systems and the concept that material, protoplasmic bodies have existed since eternity. His own hypothesis did avoid this difficulty.

**"... ob etwa die nicht organisirten todten Körper aus lebenden organisirten hervorgingen ..."

was the fact that living organisms are always descended from other living things (21). All other supposed characteristics of living things were encountered at least occasionally in the inorganic world, such as the growth and reproduction of crystals. And he considered fire, noting that it feeds itself, it metabolises and grows, it breathes the same air as we do and suffocates when air is witheld, and in the end it dies, leaving carbon behind. Yet fire is not usually considered to be alive. In addition, going back in the past, the heat that was generated by the contraction of the cooling earth must have been so high at the surface that only liquids and gases, but not solids, were present. Was there any justification for sayingthat this liquid molten mass was not alive? To Preyer, the answer was no, for we ought to take into accountthe spontaneous movement of all that is organic ("das organische Sichbewegen"). To Preyer this movement was life, and life as we know it on earth now was simply a special form of this movement (22).

Thus Preyer adopted Fechner's criterion of life as a state of motion and the idea thatthe incandescent earth was alive. He also adopted Fechner's concept of the priority of life over all inorganic matter without, however, making use of the principle of the tendency towards stability. He pictured the transition from the organic to the inorganic state on earth in very much the same way as Fechner had done before him. As the earth began to cool, those substances that could no longer remain in the liquid state separated in the form of a hard mass and became what we now call inorganic matter. The remaining liquid masses alone represented life on earth at that stage. As the solidification continued, combinations of elements appeared which until then had been in a liquid state and which gradually came to resemble protoplasm. In other words, Preyer did not maintain that protoplasm existed on earth from its very formation, nor that protoplasmic bodies had wandered onto the earth from outer space, and definitely not that protoplasm arose from inorganic matter on a lifeless earth. What he did maintain was

> "...that the eternal movement of the universe is life, that protoplasm must necessarily have remained behind when the more intense vitality of the glowing planet had caused those bodies that are now regarded as inorganic to be separated out on its cooling surface." (23)*

Once the protoplasmic residue had been left behind, Darwinian evolution and competition between organisms followed.

Finally, Preyer felt that his hypothesis had the advantage that it was nowhere contradicted by observation. If the hypothesis were accepted, all experimental attempts to demonstrate the Urzeugung would be seen to be futile and doomed to failure and the theory of cosmozoa, while not excluded, would be redundant: each planet would form its own protoplasmic remains.

According to Oparin (24), Preyer's theory had a large following but this is not apparent from the scientific literature. Those who mentioned Preyer at all had little difficulty in dismissing his views. Taschenberg felt that Preyer's concept of life was poetic but unscientific (25). Life as we know it must have had a beginning and if life were to be regarded as movement then it was a very special form of movement, associated

*"...dass die anfanglose Bewegung im Weltall Leben ist, dass das Protoplasma nothwendig übrig bleiben musste, nachdem dürch die intensivere Lebensthätigkeit des glühenden Planeten an seiner sich abkühlenden Oberfläche die jetzt als anorganisch bezeichneten Körper ausgeschieden worden waren."

with a special substrate (protoplasm). The origin of this substrate was not explained clearly by Preyer.

Verworn also criticised Preyer for stretching the concept of life so far as to include the sun and the molten mass of the early earth (26). If Preyer's concept of life were accepted, his hypothesis was not in direct conflict with the idea of the Urzeugung, which was also based on the view that protoplasmic organisms arose from the materials of the earth. On the other hand, Verworn regarded it as highly unlikely that there was an uninterrupted descent of protein from the liquid mass of the earth.

Lippmann mentioned, but did not comment on Preyer's views. He regarded the entire question of the origin of life as a problem of metaphysics rather than science (27), however, and there is no reason to believe that he considered Preyer's approach superior to any other.

Oparin commented:

> "Thus Preyer develops his deeply idealistic but very ancient conception of a universal life essence, and places an extraordinarily broad and indefinite interpretation on the idea of 'life'. If we leave out the interpretation and concern ourselves only with the question of the origin of present protoplasmic organisms, the theory has absolutely nothing concrete to offer us." (28)

Not much can be added to these comments of Preyer's critics. Merely stretching the concept of life provides no explanation for the origin of living organisms as we know them, and Preyer's ideas on the formation of protoplasm are far too vague to be of any help in this respect. As mentioned earlier, Preyer was justified in regarding the evolutionist hypothesis as ill defined. The evolutionist should be asked to define the conditions under which life could have arisen on earth. In addition, he should explain how these conditions changed with time and how the early organisms could have adapted to such changing conditions. Finally, independent evidence for the postulated conditions should be provided, for example from geology. This was an impossible task in Preyer's days in the light of the contemporary scientific knowledge. Preyer, however, regarded the task as impossible in principle. The alternative he proposed may not be contradicted by experience but that is hardly a virtue: his hypothesis is not contradicted by experience because there is no way of testing it empirically. As Oparin said, it has nothing concrete to offer.

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# CHAPTER V
## ARTIFICIAL CELL STUDIES IN RELATION TO THE PROBLEM OF THE ORIGIN OF LIFE

Evolutionary hypotheses on the origin of life postulated the primordial generation of living organisms from organic matter which had previously been formed by the gradual transformation of inorganic compounds. Hence, the continuity between the living and the non-living was seen in terms of "chemical evolution". Any qualitative differences in form and function between the animate and the inanimate were held to be the outcome of differences in the chemical constitution and complexity of the two types of structure. In the early years of the twentieth century a new approach to the problem was developed which was also based on the assumption of an evolutionary continuity between inorganic nature and living organisms. The primary emphasis here, however, was on similarities in form and function between inorganic systems and present-day living organisms rather than on continuities in chemical constitution. This new approach was inspired by previous investigations of simple models of cells such as the "artificial cells" of Moritz Traube (1826-1894).

As will be shown below, Traube believed that his model systems imitated the growth of living cells and that a study of these models could lead to an increased understanding of the physico-chemical causes of cell growth. He was extremely careful, however, not to draw unwarranted conclusions from his studies and continuously stressed the differences between his artificial cells and living cells. Some of the investigators who subsequently extended Traube's approach, on the other hand, made very far-reaching claims regarding the nature and origin of life on the basis of their results. Although Traube presented no views on the origin of life, his studies will be discussed first with a view to bringing out the full contrast between his conclusions and the extravagant claims made by a number of his successors.

The background: Traube's artificial cells

Traube's work on artificial cells arose out of his studies of plant respiration (1). He had been led to the result that the essential function of plant respiration is the oxidation of a carbohydrate dissolved in the cell sap into an insoluble precipitate, cellulose (2). If the construction and growth of cell walls in plants is the result of chemical precipitation, Traube argued, then it should be possible to reproduce this process in non-living systems.

In a preliminary communication (3) on studies of the generation of the cell membrane and of cell growth using artificial systems, Traube's argument is set out clearly. He assumed that cells grow by a process of endo-osmosis, i.e. by the influx of water due to differences in osmotic pressure between the intra- and extracellular fluids. He then considered the fact that colloids (non-crystallisable substances) cannot diffuse through colloidal membranes. In addition, if a colloid precipitate forms a cohesive skin then it should act as a colloidal membrane. On the basis of these points, Traube made the following conjecture: If a drop of a colloid A dissolved in water is introduced into an aqueous solution of a colloid B, and if A and B give an insoluble combination, then drop A will become covered with an insoluble colloidal coating. Further, if drop A is more concentrated than the surrounding solution B, then drop A will increase in size due to an endo-osmotic flow of water through the colloidal membrane.

This conjecture was confirmed by experiment. When a small drop of a solution of gelatinous glue was placed in a weak aqueous solution of tannic acid, the gelatine drop was surrounded by a glassy, transparent membrane and gradually increased in size. Subsequent experiments (4) showed that membranes could also be constructed using a colloid and a crystalloid (e.g. tannic acid and copper acetate), or even two crystalloids providing that these produce an amorphous, i.e. non-crystalline, precipitate (e.g. potassium ferrocyanide and copper sulphate). In each case, the resulting membrane was impermeable to the two starting compounds, which Traube called membrane builders ("Membranbilder") or membranogens ("Membranogene"). Every membrane had its specific permeability properties with respect to other solutes, allowing the passage of some but not of others. For example, the membrane obtained from gelatine and tannic acid was weakly permeable to a great number of simple salts while the copper ferrocyanide membrane was weakly permeable only to water, potassium chloride and ammonium chloride. From the permeability properties of his artificial membranes Traube concluded that their permeability is determined by the size of the open spaces between the molecules making up the membrane (the interstitial spaces). According to Traube, these spaces must certainly be smaller than the smallest of the two membranogens, or else we would not obtain a precipitate only at the outer surface of the cell. With regard to other solutes the membrane acts as a sieve; those solutes that are smaller than the interstitial spaces pass through, those that are larger do not.

From this view of the cell membrane as a sieve, Traube was led to his theory of membrane growth by "intussusception" (5). He had observed in living cells that the membrane does not get thinner during cell growth and concluded that the membrane does not simply stretch as the intracellular volume and the osmotic tension increase, but that new membrane material is formed during cell growth. He envisaged this process as follows: When the cell contents increase in volume by endo-osmosis, pressure is exerted on the membrane. The membrane then stretches so that the interstitial spaces become large enough to allow the passage of the smaller of the two membranogens. As soon as the two membranogens come into contact, i.e. at the cell surface, a new precipitate of membrane molecules is deposited in the interstitial spaces. In other words, membrane growth is caused by intussusception which itself is preceded and determined by endo-osmotic swelling.

In summary, Traube simulated the following processes using artificial cells: The process of membrane generation by chemical precipitation and hence the generation of enclosed cells; the process of cell growth by endo-osmosis; and the process of membrane growth by intussusception. He believed that these processes closely resembled the growth phenomena of living cells and that organic growth might rest on the same principles. However, he stressed again and again the limitations of his studies and pointed out that they provided no information regarding other essential functions of living cells, such as the role of the nucleus or cell multiplication (6). In particular, he emphasised that any conclusions drawn from his work about living cells would only apply given the pre-existence of protoplasm. He denied that his studies could throw any light on the question how living cells might be generated from non-living material, adding

> "...it was far removed from my intentions to pursue such a utopian aim..."*(7)

Stimulated by Traube's studies, other investigators used analogous models to reproduce such processes as cellular movement, phagocytosis and cell division ( 8). For example, Otto Bütschli (1848-1920) prepared oil emulsions ("microscopic foams") to see if these would simulate the properties of protoplasm (9). His choice of "microscopic foams" was based on his theory of the alveolar structure of protoplasm, according to which protoplasm is a two-phase system showing an alveolar or "honeycomb" structure resembling the microscopic appearance of oil lather.

Bütschli first prepared a thick paste by rubbing a finely pulverised soluble substance such as cooking salt or potash (potassium carbonate) into a drop of olive oil. Upon mixing a drop of this paste with a drop of water, a fine froth was obtained revealing an active exchange of water between the two phases (shown up by mixing the water with Indian ink). According to Bütschli, the streaming movements in the foam bubbles closely resembled protoplasmic streaming in plants. In addition, the moving drops became distended locally so that they resembled amoebae with pseudopodia. Bütschli explained the streaming movements in the oil lather on the basis of local differences in surface tension. Their great similarities to amoeboid movement led him to conclude

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*"...einem so utopischen Ziel nachzugehen lag mir fern..."

that similar forces must be at work in both cases. Like Traube, however, Bütschli drew no further conclusions from his studies and did not regard his oil emulsions as alive in any sense. In fact, he regretted the use of the term "artificial amoebae" for the oil foams which had been introduced by others writing about his work (10).

It may be argued that Traube and Bütschli, despite their caution, were simply wrong in suggesting that organic growth is fundamentally an osmotic process or that cellular movement is solely determined by surface tension. Certainly, their models were over-simplified and many additional forces are now understood to be responsible for such phenomena, for instance the active transport of metabolites through the cell membrane, numerous metabolic transformations catalysed by enzymes, protein synthesis directed by nuclear DNA, and bioenergetic processes. However, considering the state of biochemical and biophysical knowledge at the time, the investigations of Traube and Bütschli represented legitimate attempts at clarifying the possible role of certain simple physical processes in living organisms. Osmosis and surface tension do play an important role in living beings and are worthy of investigation. The discovery of, for example, active transport meant that an additional process had to be taken into account, not that osmosis and passive diffusion could henceforth be ignored as being devoid of any significance in living cells.

Because Traube and Bütschli were well aware of the differences between their model systems and living cells they did not make the mistake of regarding either osmosis or surface tension as the fundamental life process, unlike some of their followers. For example, Stephane Leduc, whose work will be discussed next, maintained on the basis of experiments derived from those of Traube that osmosis is the prime phenomenon of life.

Leduc's osmotic growths

Leduc's studies formed part of an ambitious programme to which he gave the name of "synthetic biology" (11). He argued that each science goes through three consecutive phases: a phase of observation and description, a phase of analysis of the observed phenomena, and a synthetic phase involving the simulation of the processes under study. According to Leduc, the biological sciences had made important advances in the description and analysis of biological phenomena whereas the synthetic phase had barely begun. He believed that the time was ripe to introduce synthetic biology, its role being

> "...to reproduce the substances, the form, and phenomena which have been the subject of investigation."(12)

For example, if the living organism was regarded as a transformer of energy*, then it should be the task of synthetic biology to reproduce similar transformations of energy outside living organisms. Leduc argued that synthetic biology had two priorities, corresponding to the two fundamental properties of living beings, nutrition and form. The argument ran as follows: The primary function of all organisms is the transformation of matter and energy. Maintaining this function, and life itself, requires the continuous supply of nutrients (in liquid form, to aid absorption). Hence, nutrition is the essential phenomenon of life and the elementary physical phenomenon is the contact between an alimentary

*Leduc was thinking of the use by organisms of energy stored in nutrients for life functions such as movement. He regarded this as a transformation of potential energy into what he called "actual" energy (13).

liquid and a cell. The study of life should therefore begin with an investigation of the physicochemical phenomena resulting from the contact between two liquids, such as solution, diffusion, osmosis, cohesion and crystallisation (14). Secondly, the essential characteristic of an organism is its form. Unlike the matter and energy circulating within it, which in its ultimate form is indestructible, the form of an individual is transitory in nature - the individual perishes with its form. Hence, it is the task of synthetic biology to elucidate the physicochemical forces and conditions which can produce forms and structures resembling those of living beings.

It so happened that in Leduc's studies the two major aims of synthetic biology converged. In his studies of diffusion, Leduc produced diffusion patterns on gelatine which resembled fern-like structures (using, for instance, concentrated solutions of silver nitrate and ammonium bromide). In his studies of osmosis, he not only produced artificial cells similar to those of Traube but, by experimenting with various salt solutions at different concentrations, much more complex "growths" resembling fungi, mushrooms, cells and plants. Some structures were green, by the use of ferrosulphate, some partly white and partly yellow, by the use of manganese salts. Besides the striking resemblances in appearance, as illustrated by the numerous photographs presented in his books, Leduc noted the following analogies between his "osmotic growths" and living organisms. First, analogies of a structural organisation: the osmotic growths are groups of cells separated by an osmotic membrane. Secondly, analogies of function, namely nutrition (the growths absorb substances from the surrounding medium and waste products are ejected), morphological differentiation, and even ageing:

> "The plumpness of a child and the turgescence of young cells are but the expression of high osmotic tension, while relaxation and flaccidity of the tissues in old age betrays the fall of osmotic pressure in the intra-cellular tissues."(15)

Finally, the osmotic growths die by disintegration.*

On the basis of these observations, Leduc reached the following conclusion:

> "Diffusion and osmosis are the elementary phenomena of life. All vital phenomena result from the contact of two colloidal solutions, or of two liquids separated by an osmotic membrane. Hence the study of the physics of diffusion and osmosis is the very basis of synthetic biology."(20)

To those who might object that the osmotic growths did not contain albumin and were therefore not comparable with living organisms, Leduc replied that such objections would be based on a confusion of life with a substance and of the synthesis of life with the synthesis of albumin. According to Leduc, life is not a substance but a mechanical phenomenon. However, when discussing the implications of his results for the question of the origin of life (21), Leduc could not entirely ignore the chemical constituents of present-day organisms. He believed thatthe accumulation of mineral and protein matter in the primaeval seas gave rise to

*Leduc himself gave no indication of the "life-span" of his osmotic growths. In a review of the subject, however, Benedikt (16) mentioned the ephemeral nature of these structures. He wrote of "ephemeral phantoms which, from the beginning, have passed in front of man's eyes without being perceived and which Leduc has managed to capture by photographic means" ("...des fantômes éphémères, qui, depuis l'origine, étaient passés devant les yeux des hommes sans être apperçus, et que Leduc a su surprendre par la photographie."). It should be added that Benedikt's remark was not intended as a criticism - he had great admiration for the clarity and simplicity of Leduc's studies.
Benedikt's review also includes photographs of structures resembling diatoms and radiolaria, obtained by the use of silicates by the Mexican biologist Herrera. Herrera's study of the life-like behaviour of artefacts, or "plasmogeny" (17), continued into the 1940s (18). Oparin recounts how Herrera sent him microscopic slides of artefacts in the late 1930s and how these were identified as living cells (and even classified) by an eminent microscopist (19).

conditions that were favourable for the production of osmotic growths. Of these, the mineral growths may have left remains that could be of interest to the geologist, while the organic growths subsequently evolved into present-day organisms. In view of the great variety and complexity of artificially produced osmotic growths, Leduc believed that the beginning of life may not have been the generation of a simple primitive cell from which all other organisms have descended, but that there may have been a variety of such primordial forms, some of them quite complex.

It should be noted that Leduc, while stressing the resemblances between the osmotic growths and living systems, did not claim to have synthesised any living organisms. With regard to the origin of life, Leduc obviously saw primaeval osmotic growths produced from protein matter as the precursors of existing organisms, and not growths of the type produced by himself in the laboratory. He did, however, regard osmosis as the fundamental force which organises matter and maintains the functions of life. The idea that osmotic forces alone could, under any circumstances, have led to the first generation of living organisms was a gross over-simplification even in Leduc's day. More important, however, is the fact that Leduc's theory failed to explain why this force, if it is <u>fundamental</u> to the origin and maintenance of life, should have given rise to both living and non-living structures. It may be that the organic osmotic growths in the primaeval seas were longer lived than mineral growths and simply won out in natural selection but Leduc provided no explanation for this supposed persistence and evolution of organic osmotic growths. At this point, his decision to de-emphasise the differences in chemical constitution between living and non-living systems entailed a petitio principi. In the history of biology, attempts to provide explanations of vital phenomena in terms of physics and chemistry have led to an ever-increasing insight into many of these phenomena. In any hypothesis on the origin of life, however, it is not enough to explain the similarities between the living and the non-living in physicochemical terms, but also the differences.

Kuckuck's barium cytodes

Leduc did not suggest that he had succeeded in synthesising living organisms or any direct precursors of existing organisms. In this respect, his conclusions were exceedingly restrained in comparison with those of Martin Kuckuck, a physician in St. Petersburgh. Kuckuck claimed to have produced living organisms that were identical to the immediate precursors of the nucleated cells of the Metazoa, and to have solved the problem of the origin of life. His ideas and experimental results, obtained from 1905 onwards, are presented in a large book entitled l'Univers, Être Vivant (22). Kuckuck's work was inspired by the studies of Raphael Dubois, Professor at Lyons, to whom the book is dedicated. Dubois had produced particles that were supposedly identical to bacterial cells by adding barium or radium chloride to a sterilised fish broth (23). The main difference between Dubois' experiments and those of Traube and Leduc, therefore, was the use by Dubois of a medium composed of material derived from living organisms. Kuckuck believed that the radium and barium had somehow "organised" this organic material into living "cytodes" (non-nucleated cells), and attributed this organising force to the ionising properties of radium and barium. His ionisation theory was formulated as follows: In plants and animals, living substance is grouped around centres of attraction consisting of ions (in the case of cytodes) or of complexes of protein molecules associated with electrolyte ions (in the case of nucleated cells). With the aid of ionising substances such as radium and barium, protein gels can be organised so that the mass of molecules becomes an integrated unit or organism. On the basis of this theory Kuckuck could solve the problem of the origin of life:

> "There, then, is the entire mystery of the generation of the first protoplasmic cells on our planet; it consists merely in the transformation of inert amorphous proteins into active structured proteins - into protoplasm, by the ionising substances." (24)*

Kuckuck's own experiments were similar to those of Dubois except for the use of a different medium, consisting of gelatine, peptone, glycerine and asparagine dissolved in sterilised sea water. When this mixture was "ionised" by the addition of barium chloride Kuckuck obtained

> "...structures that were morphologically identical to round animal cells."** (25)

These bodies, called "barium cytodes" by Kuckuck, took in "food stuffs" and exhibited growth, reproduction by segmentation, rotatory movement***, and the capacity to form groups or colonies. Furthermore, these phenomena alledgedly ceased upon addition of a poison to the medium. To Kuckuck these facts showed that the barium cytodes were alive. Considering the morphological and

*"Voilà tout le mystère de la naissance des premières cellules protoplasmiques sur nôtre planète; il ne consiste que dans la transformation des protéines amorphes inertes en protéines formées actives - en protoplasme, par les substances ionisantes."

**"..des formations morphologiquement identiques aux cellules animaux rondes."

***Kuckuck's description of the movements of the barium cytodes would be consistent with the possibility that these represented Brownian motion, especially as the movements ceased after the corpuscles had grown to a certain size.

physiological properties of the cytodes, Kuckuck was led to conclude that they must be the primordial living animal cells and felt justified in giving his "organisms" the name of "Rhizopode de baryum M.K.". Colonies of the latter closely resembled Metazoa except for the fact that Metazoa are composed of nucleated cells while his cytodes had no nuclei. According to Kuckuck, this difference proved that "Rhizopode de Baryum M.K." was the precursor of all Metazoa. He postulated the existence on the primitive earth of a second cytode, smaller than the barium cytode and containing nucleoprotein, to explain the genesis of the nucleated cell on the basis of a symbiosis of the two types of primordial cytodes (26).

As Leduc regarded osmosis as the primary force in the generation of living organisms, so Kuckuck held that life started by the action of ionising forces. Neither Leduc nor Kuckuck claimed that the fundamental force, whether it be osmosis or ionisation, was restricted to the organic domain, however, which leaves us with a dilemma. If the elementary force is both necessary and sufficient for the generation of life, an explanation must be found for the existence of inanimate objects in the sphere of influence of the vitalising force. If, on the other hand, the force is necessary but not sufficient to give rise to life, then it cannot be claimed legitimately that a complete solution to the problem of the origin of life has been given. It is then necessary to define the differences in conditions under which the fundamental forces give rise to living systems on the one hand and to non-living structures on the other hand.

Kuckuck tried to circumvent this problem by declaring the whole universe to be alive: the aether was the prime living material on account of its "ionising forces" and all cosmic bodies, including the earth and its inhabitants, were the organs of the universe. On this view, the question of the origin of life loses its meaning - the ionising forces simply vitalise everything. However, Kuckuck claimed to have given a solution to the problem of the origin of life in its usual sense, in terms of the generation of barium cytodes assuming the pre-existence of protein matter. But how did this protein matter arise in the first place? And what was the basis of the differences between protoplasmic bodies and non-protoplasmic bodies? In relation to this question, it is irrelevant whether the latter be called alive or not - merely stretching the concept of life does not make the two identical.

Butler Burke's radiobes

Views on the nature and origin of life somewhat similar to those of Kuckuck were presented in 1906 by the Cambridge physicist John Butler Burke who, however, considered the fundamental life force to be akin to, although not identical with, radioactivity (27). Butler Burke's studies were inspired in the first instance by Pflüger's cyanogen theory and only secondarily by previous studies of artificial cells. He argued that, if cyanogen is a living thing, then it should grow and multiply on a suitable culture medium*. Experiments to test this hypothesis gave negative results. Butler Burke then argued that similar experiments might

*This argument reflects a gross misunderstanding of Pflüger's theory. Pflüger did not regard cyanogen as alive but believed that the CN-radical was the essential component of "living protein". Further, Pflüger regarded complexes of "living proteins" as the essential constituents of living organisms but never claimed that any single living protein was itself an organism capable of growth and multiplication.

lead to positive results if radium were used instead of cyanogen, considering the analogies between the two substances with respect to instability and the energy stored up in them*. Accordingly, he sterilised stoppered tubes containing "bouillon" and radium chloride or radium bromide, by heating under pressure followed by rapid cooling (28). Upon cooling, the bouillon coagulated and after 24 hours a "culture" started to grow on the surface of the gelatine. Controls without radium produced no cultures, thus ruling out the possibility of bacterial contamination. After about 6 weeks the original bodies had grown in size, though to greatly varying extents, and when examined under the microscope resembled diplococci. At first they did not reveal any visible structures but later "nuclei" appeared, followed by segmentation effects after further growth. Finally, when the corpuscles had reached a certain size, they tended to subdivide and eventually they disintegrated.

Butler Burke noted the following (not insignificant) differences between his bodies and bacteria: they appeared to have originated by continuous growth from submicroscopic particles; they melted in warm water of 25° to 30°C; and, when inoculated in fresh media, the subcultures showed no sign of growth even after 6 weeks. Not easily discouraged, Butler Burke nevertheless believed that the "radiobes", as he called them, were in some sense alive and might be a primitive form of bacilli**. To support this view he considered the criteria of vitality for existing life forms, namely

*It should be kept in mind that radioactivity was poorly understood at the time.

**It is not clear why he chose the term "primitive bacilli" when the radiobes resembled diplococci.

the presence of protoplasm, metabolism, a "cyclic process" (development, growth and decay), a certain organisation and structure, dependence on temperature and moisture, and a high susceptibility to external influences. However, argued Butler Burke, it is possible that protoplasm was not essential for life forms that have not survived to the present day, but was simply the most efficient vehicle for the propagation of vital processes. If all other vital phenomena could be reproduced in non-protoplasmic bodies, then it should be concluded that protoplasm is not essential for all life and that a broader definition of life is required. Butler Burke felt that the real test of life is the "cyclic" process of development, growth and decay, and claimed that his radiobes fulfilled this requirement. Therefore, the radiobes, while not being bacteria, were not altogether lifeless and might represent the missing link between the animate and inanimate.

To Butler Burke this result had important implications for the question of the origin of life. He postulated that the radium atom could act as a nucleus which may, in a suitable medium containing the constituents of protoplasm, assume in the molecules around it the definite and unstable forms that are associated with living things:

> "The properties we call 'vital' appear to be associated with the radium emanation which, in the water from springs, or in the earth itself, may have been the cause 'through the prodigious vista of the past' of the commencement of life upon our planet." (29)

Eventually, however, Butler Burke concluded that the formation of his radiobes was not determined by radioactivity itself. He knew that Raphael Dubois had obtained somewhat similar bodies when either radium chloride or barium chloride was introduced in a gelatinous medium. The fact that non-radioactive barium gave similar results to radium suggested to Butler Burke that the formation of these growths might not depend on the intensity of radiation itself but on

> "...the process upon which radioactivity depends." (30)

He had, incidentally, confirmed himself that no cultures were produced on radiation alone - actual contact between the bouillon and the radium was required for the growth of radiobes. But even if the life force was not the same as radioactivity,

> "...life activity and radio-activity should admit of continuity." (31)

On the basis of this idea, Butler Burke suggested that the substance of the cell nucleus consists of an element or substance which possesses a store of energy comparable to the emanation from radium, and that this substance gives rise to the vital processes. He proposed to call this substance "bio-carbon", which would possess the chemical properties of carbon and, in addition, a considerable store of energy which,

> "...strictly speaking, would be energy stored in the aether and apparently at least independent of physical forces, but in reality forming a part of the dynamical connections of the universe." (32)

In other words, the source of life would be immaterial but would not transcend physical law. In this manner, Butler Burke claimed to have reconciled the materialistic and idealistic views of life, although in reality he came out strongly in favour of idealism by concluding that the atoms of which matter is composed are perceptions or spirits. He even claimed to be able to reconcile materialism and theism by suggesting that the play of physical forces be regarded as the mode of action of the Divine Mind. It is not clear how any materialist could be reconciled to this "new monism" according to which mind was fundamental.

From the descriptions given, it is difficult to tell exactly how the "cells" of Kuckuck and Butler Burke were formed. Butler Burke pointed out that Dubois never presented the details of his procedure of sterilisation and suggested that the possibility of bacterial contamination should be kept in mind. Kuckuck also mentioned sterilisation only in passing and similar suspicions might be felt in relation to his work. On the other hand, the "cultures" could well have been microscopic colloidal vesicles not unlike Traube's artificial cells. The latter explanation seems most plausible in the case of Butler Burke's radiobes in view of the precautions taken to exclude contamination and especially in view of the considerable differences between radiobes and microbes stressed by Butler Burke himself.

Neither Kuckuck nor Butler Burke attempted to investigate the chemical composition of their "cells" and, in any case, the outcome of such investigations would not have been regarded as particularly relevant by either. The chemical constitution of existing organisms appears to have been seen as incidental rather than fundamental. As a result, the origin of life was explained in terms of "forces" - Leduc's physical force of osmosis, Kuckuck's omnipresent vital force of ionisation, and Butler Burke's force akin to radioactivity which in the final analysis turned out to be a "mind force". To all three investigators, the living and the non-living (in their usual sense) were continuous but none of the theories provided a satisfactory (or any) explanation for the differences between the two and hence could not account for any transition from the one to the other in concrete terms. It must therefore be concluded that the work discussed here, despite the claims of the authors, failed to throw any new light on the question of the nature and origin of life.

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## Chapter VI
## MATERIALISM AND THE ORIGIN OF LIFE: I. HAECKEL AND HIS CRITICS

The approaches to the problem of the origin of life that have been discussed so far were noted more for their philosophical than for their scientific content. To conclude the first part of this thesis it would therefore be in order to examine more closely some of the philosophical issues that surrounded the question during the relevant period. The materialistic basis of theories of abiogenesis in particular gave rise to much controversy, especially with regard to the work of Ernst Haeckel. His scientific and philosophical writings and the reactions they provoked provide ample material for a case history of this issue.

Ernst Haeckel's hypothesis on the origin of life was based on the postulate that there is no fundamental discontinuity between the living and the non-living world or, in epistemological terms, that vital phenomena can be explained by the same laws as non-living phenomena. Applied to the problem of the origin of life, this principle led Haeckel to the view that a transition of inorganic into organic compounds must have taken place under the conditions of the prebiotic earth; that the latter were subsequently organised into albuminous matter which grew gradually into "structureless lumps of protein"; and that these protein globules represented the first living organisms, resembling present-day non-nucleated microorganisms or "Monera".

Haeckel's monistic philosophy further asserted that consciousness emerged gradually with the evolution of the central nervous system. He held that matter existed prior to mind and that mind was dependent on matter. In conjunction with his hypothesis on the origin of life, this view implied that human consciousness had its ultimate historical origin in lifeless matter.

Haeckel's account of the origin of life was criticised strongly from two opposing points of view, namely idealism and dialectical materialism. Idealist scientists who regarded mind or life as the basic substratum of reality attacked Haeckel's materialism. In this case the disagreement was not confined to the question of the origin of life as such and was clearly more fundamental. In the case of dialectical materialist criticism, on the other hand, the issues are more complex. At first sight, Haeckel's hypothesis appears to be a direct, if primitive, precursor of Oparin's theory of the origin of life. Oparin himself, however, criticised the "crude mechanicism" or "vulgar materialism" of Haeckel's approach to the problem. By the standards of scientific knowledge available to Oparin in the 1930s, Haeckel's hypothesis was indeed crude and over-simplified but the question may be raised whether this over-simplification was primarily a result of limitations imposed by Haeckel's methodology or whether it was due mainly to a lack of relevant scientific knowledge in Haeckel's days. It is hoped that an investigation of this question may contribute towards an explanation of the success of Oparin's own approach to the problem of the origin of life. In addition, the issues raised may be relevant in the context of present-day controversies between reductionism and materialistic holism in biology.

Haeckel's monistic philosophy

In order to understand many of the criticisms directed against Haeckel's theory of the origin of life, the latter must be seen in the wider context of his philosophy of nature of which it formed an integral part. The most comprehensive statement of Haeckel's philosophy is given in his Riddle of the Universe (1), first published in German in 1899. In this book, Haeckel described the triumphant march of 19th-century science and utilised its results to give support to his monistic interpretation of the cosmos.

According to Haeckel, the conflict between monism and dualism had been the major issue in philosophy throughout history. Dualism, which breaks up the universe into two entirely distinct substances, separates the material world and its immaterial creator, or body and spirit, or matter and energy, and is traditionally associated with teleological or idealist "dogmas" (2). Monism, on the other hand, recognises one sole substance in the universe, regards the dualist's antitheses as inseparable, and favours mechanical and realistic theories (3).

Haeckel believed that the scientific knowledge accumulated over the 19th century gave indubitable support to the notion of the unity of nature, that is to say, to the notion that all phenomena in the universe stand in causal connection and can be explained by one set of natural laws. He based his monism on three laws which he regarded as universal: the law of substance, the law of evolution and the law of causality. The law of substance (4) was a combination of the laws of conservation of matter and conservation of energy. Substance, to Haeckel, was the fundamental substratum of existence and the conservation laws suggested that substance has two attributes, matter and force or energy. (The latter two terms were used interchangeably by Haeckel.) These attributes could not exist or be operative independently: there is no such thing as inert matter, i.e. matter that can only be moved by extrinsic forces, and there are no immaterial forces at work in nature. Hence, Haeckel rejected spiritualism, in which mind or spirit is fundamental, as well as Ostwald's energism in which matter is regarded as a product of energy (5). At the same time, Haeckel rejected the consistent materialism of, for example, Democritus who made matter precede force. He favoured the system of the Presocratic philosopher Empedocles, according to which the basic elements have intrinsic affinities of "love and strife" or attraction and repulsion; and he noted that the varying intensity of combinations between chemical elements ranged from "complete indifference to the fiercest passion" (6). Thus, the atoms themselves were regarded by Haeckel as having a rudimentary form of sensation or feeling ("aesthesis") and will or inclination ("tropesis") (7).

In The Riddle of the Universe Haeckel set out to demonstrate that his notion of substance, supplemented by the concept of evolution and the principle of causality, provided a solution to all major "riddles" except one. In the final analysis, one problem remained, namely the question of the essence of substance which, in Haeckel's opinion, could be left to be dealt with by the metaphysician (8). In particular, Haeckel addressed himself to the questions posed by Emil Du Bois-Reymond in his lecture entitled The Seven Riddles of the Universe (9). According to Du Bois-Reymond, the following major problems remained to be settled in so far as they were capable of solution at all (10):

(i) The nature of matter and force

(ii) The origin of motion

(iii) The origin of life

(iv) The (apparently pre-ordained) orderly arrangement of nature

(v) The origin of simple sensation and consciousness

(vi) Rational thought and the origin of speech

(vii) The freedom of the will

Du Bois-Reymond believed that the first, second, fifth and possibly the seventh of these problems were in principle incapable of solution in that they transcend the inherent limitations of human understanding. He regarded the remaining questions as extremely difficult and as yet totally obscure, but in principle intelligible in scientific terms. Haeckel, on the other hand, took a more optimistic view. He claimed that Du Bois-Reymond's first, second and fifth problems had been settled by his (Haeckel's) notion of substance; that the third, fourth and sixth questions had been "decisively answered" by the theory of cosmic and organic evolution; and that the question of the freedom of the will was not an object for critical scientific enquiry because it has no real existence (11).

Haeckel's first claim may be criticised on the grounds that his notion of substance did not so much settle the three questions under discussion as reduce them to one single problem, the problem of the nature and origin of substance: The question of the nature of matter and force is reduced to that of the nature of substance because matter and force are the two attributes of substance. All forms of energy, according to Haeckel, are modes of motion;

hence motion is an inherent property of substance and the question of the origin of motion is reducible to the problem of the origin of substance (12). Similarly, it is the energy inherent in substance that endows the latter with "sensation", so that the origin of sensation is again reducible to the basic problem of substance. As mentioned previously, Haeckel regarded the problem of the essence of substance as metaphysical, thus acknowledging the existence of one fundamental enigma not capable of scientific solution.

Haeckel's views on the remaining "riddles" will now be discussed in turn. His views on the problem of the origin of life have been discussed in detail previously (see Chapter II of this thesis). While Haeckel admitted that he had not provided a final solution to this problem in all its detail and complexity, he disagreed with Du Bois-Reymond's verdict that the question was as yet totally obscure. Haeckel maintained that, with the aid of his monistic scheme, he could suggest the correct approach to the problem and locate the precise points which required explanation. In order to form a bridge between the Kant-Laplace theory of stellar and planetary evolution and Darwin's theory of organic evolution, it was necessary to seek the answer in a gradual transition from inorganic to living matter by physicochemical causes at a stage when conditions on the earth's surface were favourable. The crucial step in this transition was seen to be the formation of protein because Haeckel believed all vital phenomena to be the result of the peculiar properties of protein matter. Hence, the main priority in the solution of the problem of the origin of life was to be the elucidation of protein structure and its artificial synthesis by the organic chemist. From the formation of protein onwards, the transition from non-life to life was relatively straightforward according to Haeckel. Protein matter would form aggregates of high complexity at the molecular level but as yet undifferentiated in a morphological sense. Once an individual aggregate had grown beyond the limits of stability it would divide into two by simple cleavage, at which stage the "lump of protein" was to be regarded as a simple organism capable of reproduction (a "Moneron"). Cells evolved from the simplest Monera by the formation of a membrane (by condensation of the outer layer of plasma or by deposition of an outer covering) and a nucleus (by condensation of the inner kernel of plasma). From the cellular stage, diverse and complex forms of life evolved by natural selection and adaptation, as explained by Darwin.

To Haeckel, the orderly arrangement of nature was by no means pre-ordained. Kant and Laplace had explained the origin and constitution of planetary systems by means of mathematical and physical laws (13). And Darwin's contribution had been precisely to explain the apparent purposiveness of organic evolution in "mechanical" terms. In Haeckel's words:

> "The struggle for life is itself a mechanical process, in which natural selection uses the disproportion between the excess of germs and the restricted means of existence, in conjunction with the variability of species, in order to produce new purposive structures mechanically and without any preconceived design." (14)

The issues of the origin of consciousness and of rational thought were, to Haeckel, but two aspects of the general problem of the psychic activity of the organic world. He regarded psychic activity as a group of phenomena dependent on a definite material substratum which he called "psychoplasm" and which he classified as a type of protoplasm (15). The lowly psychic life of unicellular organisms, plants and lower animals (expressed as irritability, reflex movements, sensitivity and the instinct of self-preservation) was directly determined by physiological action in the whole protoplasm, that is to say, by physical and chemical changes due partly to heredity and partly to adaptation. According to Haeckel, the situation could not be essentially different in higher animals and man, for the latter had evolved from the lower organisms. Man's psychic activity represented merely a higher degree of integration and centralisation. The task of psychology, then, was

> "...the objective, comparative study of the long gradation by which man has slowly arisen through a vast series of lower animal conditions." (16)

Haeckel recognised the following chief stages in this historical development, each stage being reached by progressive heredity and functional adaptation: (i) the sensitivity and movement of the entire protoplasm; (ii) the differentiation of psychoplasm from the rest of protoplasm, associated with the development of very simple and undiscriminating sense organs such as pigment spots; (iii) the differentiation of the "neuroplasm", associated with the development of a nerve network and specific sense organs of smell, taste, touch, temperature, hearing and sight; (iv) the centralisation or integration of the nervous system which gradually gave rise to consciousness; and (v) the differentiation of specific organs of thought (the "phronema") in man and the higher animals (17). The development of higher intellect and reason in man was intimately connected with the rise of language, said Haeckel. But here again, there was a long, unbroken chain of development, speech not being the prerogative of man. Only man developed articulate conceptual language but, according to Haeckel, this is a difference of degree, not of kind (18).

Haeckel held that the unconscious psychic phenomena of unicellular organisms (or "cell soul") connected the chemical processes of the inorganic world with the highest mental activities of man (19). This view was given more elaborate expression in his later book The Wonders of Life (20), described as a necessary supplement to The Riddle of the Universe. In this work, Haeckel listed sensation as a third attribute of substance because the simplest form of sensation was common to organic and inorganic bodies:

> "...sensitiveness is really a fundamental property of all matter, or, more correctly, all substance." (21)

Chemical sensation, for example was the basis of all chemical affinity, and atoms might be said to have a "soul". Haeckel presented a "scale of sensation and irritability" consisting of twelve steps, starting with the sensation of atoms, going via the sensation of cells, and the sensation of animals with a differentiated nervous system but without consciousness, to sensation with consciousness and thought (exhibited by "amniotes, higher reptiles, birds and mammals:savages") and finally to sensation with productive action in art and science, which was the prerogative of "civilised men" (22).

Haeckel did not, of course, claim to have explained the workings of consciousness or of rational thought simply by proposing this scheme. Yet he believed that his comparative and phylogenetic approach to the problem showed that all mental activity depends on physical and chemical processes in material substrata and that it is elevated to more complex levels by progressive evolution. Hence, there was no fundamental enigma, but a series of complex scientific problems requiring extensive further investigation. The problem of consciousness in particular was regarded as an extraordinarily difficult subject, our only source of knowledge of consciousness being that faculty itself. Haeckel insisted, however, that the centralisation of the nervous system was an absolute condition of consciousness. Progress could be made by localising the "thought centres" and "sense centres" of the brain. Pathological studies, for example, had already shown that injuries of a certain part of the human brain could affect the faculty of speech. In addition, various chemicals such as alcohol, ether, chloroform, coffee and tea were known to have specific effects on mental activity, which would be inexplicable if consciousness were an immaterial entity, independent of anatomical organs (23).

Du Bois Reymond's final riddle of the freedom of the will was dismissed by Haeckel as an illusion. He held that

> "...each act of the will is as fatally determined by the organisation of the individual and as dependent on the momentary condition of his environment as every other psychic activity". (24)

In other words, the character of our inclination is determined by heredity while each particular act is determined by adaptation of this general inclination to particular external conditions.

Haeckel's entire scheme was rigidly deterministic. According to the general law of causality, every phenomenon has a mechanical cause and in this sense there was no such thing as chance. Haeckel felt it useful to retain the term chance, however, to express the simultaneous occurrence of two events that were not causally related to each other but of which each had its own mechanical cause, independent of the other (25). For example, Haeckel believed that protoplasm and Monera were likely to have evolved on any planet covered by large amounts of liquid water, due to the inherent properties of carbon compounds. On the other hand, he thought it questionable whether the development of higher animals would have taken a similar course on the earth and other planets, for this would presuppose that millions of changes had been the same in each situation (26). In this sense, the evolution of man was contingent rather than necessary, but not strictly due to chance.

Thus, Haeckel's monism was developed into a vast scheme of cosmic evolution in which human history represented an evanescently brief episode; and

> "...as our mother earth is a mere speck in the sunbeam in the illimitable universe, so man himself is but a tiny grain of protoplasm in the perishable framework of organic nature." (27)

Consistent with this view, Haeckel held that there exists an external reality independent of man's consciousness. He rejected both Berkeleyan idealism and the Kantian notion of the "thing in itself" (28), of which he later wrote:

> "This dogma is erroneously built on the correct idea that our knowledge, obtained through the senses, is imperfect; it extends only so far as the specific energy of the senses and the structure of the phronema admit. But it by no means follows that it is a mere

> illusion, and least of all that the external world exists only in our ideas... Space and time are not merely necessary forms of intuition for human knowledge, but real features of things, existing quite independently of perception." (29)

According to Haeckel, sense experience is the ultimate basis of all our knowledge; what may appear to be an innate capacity, or an _a priori_ quality, of our understanding is really a phylogenetic result of a long series of brain adaptations, based on _a posteriori_ sense perception and experience (30). In other words, Haeckel believed that _a posteriori_ knowledge could gradually become _a priori_ knowledge by inheritance (31).

However, Haeckel did not believe that immediate sense experience was sufficient in itself for the understanding of reality, but that experience or observation and thought or speculation were of equal value and mutually complementary (32). Sense experience alone would never provide us with a complete philosophy while pure speculation was apt to lead to idealism, as in the case of Plato or Hegel. Only a combination of the two distinct cerebral functions would lead to the acquisition of true knowledge. Thus Haeckel avoided extreme positivism.

Monism, according to Haeckel, was generally associated with both realism and mechanism, but he interpreted mechanism in the very wide sense of being "not teleology". He rejected all teleological explanations in terms of final causes, for he wished to avoid the dualistic notion of a "wise providence" guiding the destiny of all things and beings (33). Instead, he insisted that explanations in terms of efficient causes be sought everywhere, and labelled such explanations as mechanical, causal or monistic*(34). To Haeckel, then, a mechanical explanation did not necessarily involve a full reduction to physical processes. For example, he criticised the so-called exact (according to Haeckel pseudo-mechanical) method in embryology on the grounds that it attempted to reduce complex historical processes to simple physical phenomena, such as the bending and folding of elastic plates, the hollowing out of vesicles, etc. (35). Haeckel believed that there was a direct causal link between the observed facts of embryology and the theoretical ancestry of any species, and expressed this "mechanical causal nexus" in his biogenetic law: "Ontogeny is a brief and imperfect recapitulation of phylogeny" (36). Each process in embryological development was a recapitulation of a long series of historical changes produced by the cooperation of a vast number of instances of adaptative and hereditary change over millions of years. At the same time,

> "Naturally, each of these physiological processes has in turn been determined by mechanical causes, or by physical and chemical conditions; but these are far removed from direct and exact observation, as they are 'pre-historic' phenomena of the remote past." (37)

Hence, Haeckel included historical explanations in terms of evolutionary development under the general heading of mechanical explanations. This may explain, for example, why he claimed to have answered decisively such questions as the origin of

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*His remark, quoted above, that the struggle for life is a mechanical process should be understood in this light.

consciousness by adopting a purely comparative and phylogenetic, as opposed to a mechanistic (in its usual sense), approach.

Haeckel characterised his own monism as hylozoistic (38) because he ascribed sensation to all substance, first as a function of its inherent energy and later as one of its fundamental attributes. He also believed that his dynamic conception of substance enabled him to remove the dichotomy between theoretical materialism and theoretical idealism and combine the two into a harmonious whole (39). He did allow, however, that his monism might be equated with scientific materialism in so far as the latter holds that all nature is one and that the same laws are active throughout nature:

> "In such a sense all exact science, and the law of cause and effect at its head, is purely materialistic. But with equal justice it might be termed purely 'spiritualistic', if only, as a consequence, the monistic conception were applied to <u>all</u> phenomena without exception. For it is precisely by means of this <u>consistent unity</u> that our modern monism constitutes itself the mediator between idealism and realism, and the adjustor of one-sided spiritualism and materialism." (40)

It should be noted, however, that Haeckel's system was totally incompatible with subjective idealism or phenomenalism, because of his recognition of the independent existence of the external world, and with any form of spiritualism which postulated the priority of mind over matter. On the other hand, the main difference between Haeckel's scheme and materialism consisted in his assertion that all material entities have some form of sensation or "soul". Haeckel's interpretation of the term sensation, however, was very wide indeed. At the physicochemical level, the sensation of matter took the form of attraction and repulsion between atoms; at higher levels of complexity sensation was expressed as, for example, chemotropism in bacteria, light sensitivity in plants, reflex action in animals and conscious thought in higher animals and man. Hence, Haeckel's "hylozoism" would be consistent with a materialist philosophy which assumes the inseparability of matter and energy and regards the above "modes of sensation" as properties of specific complexes of matter-energy. As pointed out by DeGrood (41), the debate between monism and dualism was but one aspect of the deeper ideological conflict between materialism and idealism. In this respect, Haeckel's monism can justifiably be characterised as materialistic.

Finally, it should be pointed out that all of Haeckel's writings stressed the fundamental unity of nature. To Haeckel, all phenomena stood in causal relation and all historical developments were strictly continuous. By emphasising the continuity of phenomena throughout, Haeckel often appeared to deny the emergence of new qualities during the historical development of substance. For example, he continually stressed the unity of the organic and the inorganic world, finally culminating in the statement, written in 1917:

> "All substance possesses life, inorganic as well as organic; all things have soul, crystals as well as organisms."* (42)

(This view was inspired by the discovery of liquid crystals, which in Haeckel's opinion exhibited vital phenomena.) Apart from this most extreme statement of Haeckel's, however, he

*"Alle Substanz besitzt Leben, anorganische ebenso wie organische; alle Dingen sind beseelt, Kristalle so gut wie Organismen."

generally held that life was bound up with protein and rejected, for example, Preyer's extension of the concept of life to the whole cosmos:

> "This concept only increases the confusion, and the difficulty of marking off biological from abiological science, which is both practically necessary and theoretically justified." (43)

This does not mean that Haeckel regarded the transition from non-life to life as a sudden leap, but as a gradual, continuous process where it may be hard to draw a clear line of demarcation between the living and the non-living. Similarly, Haeckel held that the evolution of consciousness was intimately connected with the differentiation of the central nervous system. He did, therefore, allow for the emergence of new qualities but did not, on the whole, emphasise their novelty. To illustrate the latter point, he denied, for example, that human reason was essentially different from conscious thought in animals. He regarded reason in its widest sense to be a property common to all higher vertebrates and claimed that the highest forms of reason were lacking not only in animals but in most men as well (44). This view led him to make statements such as the following:

> "The difference between the reason of a Goethe, a Kant, a Lamarck, or a Darwin, and that of the lowest savage, a Veddah, an Akka, a native Australian, or a Patagonian, is much greater than the graduated difference between the reason of the latter and that of the most 'rational' mammals, the anthropoid apes, or even the papiomorpha, the dog, or the elephant." (45)

It should be added here that Haeckel tended to regard "savages" as living fossils (as Darwin had done before him) and ascribed cultural differences to biological differences between the various human races. In general, Haeckel tended to reduce social phenomena to biological factors and failed to draw any clear distinction between social, cultural and organic evolution, reducing all to the omni-present struggle for existence. Morality, for example, was built up by adaptation of the social mammals to the conditions of existence:

> "The morals of nations, so rich in psychological and social interest, are nothing more than social instincts, acquired by adaptation, and passed on from generation to generation by heredity.*" (46)

In conclusion, Haeckel's emphasis on continuity, on differences of degree rather than kind, tended to a blurring, and in some cases an explicit denial, of distinctions which clearly required explanation. To say that human conceptual speech is historically linked to the vocal signals of animals, for example, is a far cry from explaining the vast differences between the two. Haeckel's attempt to interpret the cosmos and its development in a manner consistent with scientific principles was a bold and in many ways admirable one, but one cannot avoid the impression that he explained away a number of important problems by hiding them under the general blanket of evolutionary continuity.

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*Haeckel believed in the inheritance of acquired characteristics. He held that evolutionary phenomena could not be explained solely in terms of causes internal to the organism, but that the concept of inheritance of acquired characteristics was required in order to do justice to the significance of environmental influences. He applied this principle to biological as well as social evolution and rejected, for example, Weismann's theory of the continuity of the germ plasm (47).

Idealist criticism of Haeckel: Sir Oliver Lodge

The Riddle of the Universe became an immediate bestseller in Germany and, upon translation, in many other countries including Britain. When Haeckel's protagonist Heinrich Schmidt published a summary of over 90 reviews of the book eight months after its appearance, 10,000 copies had already been sold (48). The English translation, published in a six-penny edition by the Rationalist Press, went through five editions in two years.

The popular success of Haeckel's book was accompanied by much fierce criticism, especially from the German philosophical establishment and from religious quarters. Haeckel's attacks on the basic tenets of the traditional Christian church and his defence of pantheism provoked great indignation*. His critique of contemporary philosophy proved equally unpalatable. The prominent Neo-Kantian philosopher Friedrich Paulsen, for example, published a highly emotional tirade against Haeckel's atheism and materialism without, however, giving any critical appraisal of Haeckel's ideas (50). After having accused Haeckel of dogmatism, of giving a caricature of Kant's philosophy, of not having a philosophical temperament, etc., Paulsen concluded as follows:

> "I have read this book with burning shame for the state of general culture and the philosophical culture of our people. That such a book was possible, that it could be written, printed, read, admired, believed by a people which claims a Kant, a Goethe, a Schopenhauer, is painful." (51)

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*Haeckel advocated the pantheistic view that God and nature are one, God being operative in the world as force or energy. At the same time, he agreed with Schopenhauer that pantheism is only a polite form of atheism because of its rejection of an extramundane deity. Haeckel formulated a "monistic religion" based on the worship of Nature (49).

Paulsen directed his wrath at "Haeckel the philosopher", not at "Haeckel the biologist"*, and his criticisms had no direct bearing on Haeckel's scientific theories or methodology. While Paulsen's views are therefore of limited interest in the present context, they illustrate the fact that Haeckel's philosophy of nature provoked immense antagonism on the part of idealist philosophers. The latter rightly regarded Haeckel's system as thoroughly materialistic despite Haeckel's own disclaimers.

The participants in the controversy surrounding The Riddle of the Universe included many scientists as well as philosophers. In a lively correspondence in The Times Lord Kelvin, for example, deplored Haeckel's mechanistic approach to biology and argued in favour of the idea of a vital principle (53). The most detailed critique of Haeckel's work by a scientist was presented by the English physicist Sir Oliver Lodge (1851-1940) in his book Life and Matter (54). Lodge described his book as an "antidote" to The Riddle of the Universe, written for the benefit particularly of "unbalanced and uncultured persons" who might be misled to believe that Haeckel's ideas represented the ultimate and final truth (55). It was Lodge's aim to meet Haeckel on scientific ground and to show where the latter had stretched scientific theory into baseless speculation, so as to reveal the weaknesses of Haeckel's system. At the same time, Lodge

*These and other labels such as "Haeckel the monist" and "Haeckel the pantheist" made J.E. Poritzky exclaim "How many Haeckels are there then?" ("Wie viele Haeckels gibt es denn?") (52).

failed to conceal his own philosophical bias and went beyond the facts in many instances where he accused Haeckel of doing exactly that, but in a different direction. Thus, Lodge came out in favour of teleology, vitalism and spiritualism rather than the agnostic view which he claimed to advocate whenever Haeckel transgressed into the unknown.

Lodge's opening attack was directed at the very basis of Haeckel's monism, namely at his notion of substance (56). Lodge agreed with Haeckel that anything which really exists must be perpetual while arbitrary collocations and accidental relations must be temporary. He denied, however, that this perpetual reality was captured adequately by Haeckel's concept of substance. First of all, Lodge wished to keep open the possibility that new forms of energy might yet be discovered and that the law of conservation of energy might be refuted at some stage. Similarly, he believed that the creation and destruction of matter might eventually prove to be within the realm of experimental possibility. In either case, Haeckel's law of substance, fundamental to his monism, would no longer be valid. Secondly, it was not at all clear to Lodge why Haeckel should regard matter and energy as one thing rather than two (57). In fact, Haeckel did not regard matter and energy as one thing but as the two attributes of one sole reality, substance; and he could characterise his system as monistic because it was based on substance alone. Haeckel did not envisage the conversion of matter into energy or vice versa; the two were inextricably linked but not identical or interconvertible*. Finally, Lodge accused Haeckel of neglecting the possibility that categories other than matter or energy might have fundamental existence. For example, life or mind might be fundamental instead of being associated only with certain complex groupings of matter as asserted by Haeckel (59).

The above criticisms already reveal the somewhat curious nature of Lodge's antidote to what he called Haeckel's "bigotry". On the one hand, Lodge questioned the ultimate validity of such well-established scientific doctrines as the laws of conservation of matter and energy in an attempt to undermine the basis of Haeckel's system. On the other hand, he was prepared to consider life as a fundamental, indestructible category of existence while admitting himself that the nature of life was as yet poorly understood (60). If it had been Lodge's sole purpose to show that alternatives to Haeckel's scheme were conceivable, his argument so far would be valid but rather trivial. It remains to be seen, however, whether Lodge succeeded in formulating an equally valid or better alternative.

Lodge's next criticisms were aimed at Haeckel's materialism, especially with regard to the question of the origin of life and the problem of consciousness. According to Lodge, it was all very well to say that the physicochemical properties of carbon confer such peculiar powers on protein matter that the

*While it is correct that Haeckel's fusion of the laws of conservation of matter and energy anticipated modern developments, as stated by DeGrood (58), Haeckel's motivation for this fusion was not based on an advanced physical interpretation of the matter-energy relationship.

latter develops into protoplasm, but this did not provide us with an understanding of life. Similarly, the assumption that all mental processes are based on a material substratum and are ultimately reducible to attraction and repulsion between atoms explained nothing about the nature of mind (61). Lodge objected in particular to Haeckel's tendency to relegate the inexplicable to the atoms:

> "Instead of tackling the difficulty where it actually occurs; instead of associating life, will, and consciousness with the organism in which they are actually found, these ideas are foisted into the atoms of matter; and then the properties which have been conferred on the atoms are denied in all essential reality to the fully developed organisms which those atoms help to compose!" (62)

Although Haeckel did not heap quite as many properties on the atoms as claimed here by Lodge, there is much justification for this criticism, particularly in regard to Haeckel's notion of sensation. Lodge pointed out that new properties, not initially present in the individual atoms, may emerge as a result of the aggregation of atoms. Haeckel did not in fact equate the "sensation" manifested by atoms and the sensation of, say, animals or human beings; but by stressing the continuity between the two he placed too little emphasis on the emergence of new qualities. In addition, Haeckel's terminology was confusing. To talk of "atom souls", for example, does not illuminate the concept of either soul or atom if it simply refers to properties of attraction and repulsion. Nevertheless, Lodge should not have overlooked the fact that Haeckel explicitly associated life and consciousness with specific aggregates of matter (protoplasm and the central nervous system respectively) and not with the atoms themselves. At the same time, the mere recognition of this fact would not have satisfied Lodge, as will become clear below.

Lodge did not only reject the idea that sensation is inherent in atoms but the more general view that all mental processes necessarily have a material basis. He admitted that the brain is the organ of mind or consciousness but added that

> "...we have not granted that mind is <u>limited</u> to its material manifestation; nor can we maintain that without matter the things we call mind, intelligence, consciousness, have no sort of existence...Mind may be incorporate or incarnate in matter, but it may also transcend it; it is through the region of ideas and the intervention of the mind that we have become aware of the existence of matter." (63)

To Lodge, the essence of mind was design or purpose and because evidence of guidance and control was all around us, he felt that it was reasonable to assume that guidance was an element running through the universe. He added:

> "Many a thinker, brooding over the phenomena of Nature, has felt that they represent the thoughts of a dominating unknown Mind partially incarnate in it all." (64)

In addition, Lodge regarded it as a fact that life itself was a guiding principle: The fact that an organism possesses life enables it to guide the elements of inorganic nature, to build up the material particles into such diverse forms as those of an oak, an eagle or a man; and these forms could persist only until the guiding principle abandoned them (65). This view led Lodge to the conclusion that life belonged to an entirely different category than matter or energy. He believed that life could interact with the material world but could also exist independently of matter. Life's essential existence was continuous and permanent while its interactions with matter were discontinuous and temporary (66). Because life dissociated from material structures could not be perceived by the senses, this also meant that life was outside the scheme of mechanics. The vital principle could direct material forces in such a manner that no mechanical laws were broken but it was not itself determined by any mechanical cause (67). Mental and vital interaction with the material world, then, was

> "...naturally and necessarily excluded from scientific method and treatises." (68)

Having placed life and mind firmly outside the realm of scientific enquiry Lodge proceeded to criticise Haeckel's materialistic approachto the problem of the origin of life (69). Lodge accepted Haeckel's account of the capacity of carbon to form complex aggregates and eventually, under appropriate conditions, protoplasmic bodies. He also accepted that at critical stages of organisation, qualitative changes accompanied the gradual quantitative building up of complex molecular structures. Thus, the simplest protoplasmic bodies could assimilate foodstuffs and reproduce by cleavage; at later stages of organisation powers of differentiation, communication and eventually self-consciousness emerged. Nevertheless, Lodge could not accept that the material aggregates themselves had generated the vital or mental activities exhibited by them. In Lodge's opinion, all that could be said was that such complex molecular structures could serve as the material frame of life while life itself might be an immaterial and ultra-terrestrial principle (70). Even if scientists in the future succeeded in generating living organisms from suitable materials, this would merely show to Lodge that appropriate vehicles for life could be synthesised artificially. The organism's vitality, on the other hand, could well have pre-existed independently,

> "...being called out, as it were, from some great reservoir or storehouse of vitality, to which, when its earthly career is ended, it will return." (71)

With this type of criticism an impasse is reached. No explanation in terms of physics and chemistry could ever account completely for the origin of life to Lodge's satisfaction because he placed life outside physics and chemistry, and outside science in general. Life and mind were relegated to the spiritual domain while science could only deal with the material world. Haeckel, on the other hand, believed that all biological and psychological phenomena were in principle capable of scientific explanation. Clearly, the metaphysical differences between Haeckel and Lodge were unbridgeable. Moreover, Lodge precluded the possibility that any empirical data might settle the conflict between their respective approaches.

Lodge claimed at the start of his book that he would meet Haeckel on scientific ground and leave out philosophical considerations. Yet Lodge seemed to go along with most of Haeckel's theories as far as the material world was concerned, pointing out only that such theories did not necessarily provide us with a complete understanding of reality. The latter proviso was not, however, based on scientific arguments but on extra-scientific beliefs. For example, Lodge was willing to accept Haeckel's account of the generation of protoplasm, adding even that such complex aggregates were likely to have properties differing not only in degree but also in kind from the properties of simpler substances. Having provided himself with a framework for explaining the vital functions of simple organisms in naturalistic terms, Lodge then immediately abandoned this approach in favour of an unknown (and to all intents and purposes unknowable) vital principle. As stated by Joseph McCabe, an expriest who translated a number of Haeckel's works into English,

> "This is a clear departure from scientific reasoning in the interest of a spiritist theory that has been set up on other grounds." (72)

If Lodge wanted to point out that Haeckel's account of the origin of life was speculative, he was right and Haeckel might not have denied the charge. But Lodge did not simply adopt an agnostic position; he rejected any mechanistic account of the problem, in defence of spiritualism. He did not, however, discuss any of the problems raised by his own approach. Why, for example, should life always be associated with protoplasm? Why should "spirit" not vitalise other structures? Do we know of any protoplasmic bodies that are notand never have been alive? Lodge avoided such questions by denying that the interactions between matter and spirit are open to scientific investigation. A similar point can be raised with respect to Lodge's interpretation of the interaction between the mind and the brain. Lodge accepted that the human brain was the organ of thought and that both the brain and intelligence had evolved gradually; yet he denied that the brain was the basis of thought. McCabe commented as follows:

> "Millions upon millions of [ganglionic] cells are woven into the gray bed or cortex of the brain, with which intelligence is associated. To say that all this complexity is only for the purpose of letting in a spiritual principle from another world is gratuitous in the extreme." (73)

Lodge made no attempt to explain why his spiritual principle should be so selective with regard to its terrestrial vehicles.

Lodge's soundest criticism of Haeckel concerned the latter's tendency to avoid problems regarding the emergence of such properties as sensation by relegating them to substance. Because Haeckel refrained from discussing the nature of substance, Lodge was correct in pointing out that such a strategy failed to explain anything about the various forms of sensation that we observe. As pointed out by Lodge, new qualities can and do emerge when complex structures are formed from simpler components*. At the same time, it is clear that Lodge did not regard life or consciousness as new properties emerging solely as a result of the material formation of protoplasm or of the brain. In addition, Lodge was guilty of the same error which Haeckel had committed in the case of sensation,

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*This was denied by Allen Clarke, a spiritualist who believed in the reincarnation of the soul. Clarke stated that science teaches us that like comes from like and hence it was impossible that "mindfull man" came from "mindless matter" (74). Clarke also ridiculed Haeckel's view that life is the result of the activity of carbon compounds and concluded that Haeckel's mind "...is nothing more than a mite of carbon - stuff you can scrape out of any chimney flue - and this man, who has nothing to think with but a speck of carbon, actually dares to reckon up the infinite universe, and to decide what is good and what is bad" (75).

when he postulated the existence of a fundamental principle of guidance. The fact that living organisms, and especially human beings, show purposive behaviour provides no justification for the assumption that the entire universe is controlled by a guiding principle, nor does it explain the purposiveness of the organisms where it is actually encountered.

Lodge's disagreement with Haeckel, then, was not primarily on the scientific level. What Lodge, like most of Haeckel's other critics, objected to was Haeckel's materialism. As mentioned previously, Haeckel had reservations about the term materialism because the latter was often interpreted as being based on matter without force ("dead atoms") while he regarded matter and force as two attributes of one fundamental reality. As pointed out by McCabe, however, every materialist at the time assumed matter to be associated with force or energy of motion (76). Hence, Haeckel's interpretation of materialism was somewhat outdated and there was no essential difference between his monism and 19th-century scientific materialism. Lodge could not refute Haeckel's materialism by scientific arguments; all he could do was to present an alternative philosophical interpretation of the questions dealt with by Haeckel. Whereas Haeckel's system was firmly based on the findings of 19th-century science, however, Lodge had to resort to unknown and unknowable principles for the foundations of his scheme. Moreover, Lodge was committed to the view that it was impossible in principle to reduce mental and vital phenomena to scientific laws regardless of any future scientific progress. Haeckel's system was much more flexible in that it was open to modification in accordance with scientific progress.

McCabe summed up Haeckel's position clearly in the following statement referring to Haeckel's theory of the origin of life, but which would apply equally well to other details of Haeckel's philosophy of nature:

> "On the one hand, there is the negative side, that we are not justified in rushing into the present gap (such as it is) of scientific knowledge with a 'vital force' or a 'creative power', which are specifically distinct from the natural forces we have hitherto studied; and there is, further, the positive attempt to sketch a theory of the way in which protoplasm was evolved. The first part is essential to Monism; the second is not, and may vary with the progress of science." (77)

Dialectical issues

Haeckel's materialistic monism was criticised not only by idealist philosophers and scientists, but also from the point of view of dialectical materialism. In the historical chapters of his book Origin of Life, Oparin attacked Haeckel's approach to the question of the origin of life, which he called "crude" and "mechanistic" (78). According to Oparin, Haeckel could see no difference between the formation of a crystal and of a living cell and believed that the simplest organisms had arisen all at once from inorganic matter (79). Haeckel had taken into account insufficiently the vast complexity of even the simplest known organisms and had replaced the historical processes leading to this complexity with the postulation of mysterious unknown physical conditions on the prebiotic earth. To Oparin this meant that Haeckel's theory of abiogenesis hardly constituted an advance over earlier beliefs in spontaneous generation, except that he confined the event to the long-distant past and substituted unknown external conditions for a vital force* (80).

In fact, Haeckel's apparent lack of insight into the complexity of the "Monera" had previously been criticised by a number of his contemporaries, for example Nägeli and Weismann (see Chapter II). In response to these criticisms, Haeckel subsequently refined his theory somewhat in The Wonders of Life where he made it clear that he did envisage a long process of chemical evolution prior to the genesis of living organisms. In particular, he now incorporated Pflüger's cyanogen theory of the formation of nitrogenous carbon compounds in his scheme (82). In addition, he admitted that some of the organisms which he had previously included among the structureless Monera (e.g. Protoamoeba and Protomyxa) had since been found to be differentiated morphologically. He insisted, however, that there are such things as Monera and attached particular significance to the unicellular algae Chromaceae (83).

Nevertheless, the theory remained vague and over-simplified by the standards of the 1930s, by which time the biochemical complexity of microorganisms was much better understood and important insight had been gained into the basic structure of proteins. Oparin himself could incorporate this newly acquired knowledge into his scheme. In addition, however, Oparin drew from many other sources, such as chemistry,

*A similar point was raised at about the same time by the French Marxist biologist Marcel Prenant who virtually equated 19th-century beliefs in abiogenesis and beliefs in spontaneous generation, and rejected both (81). He also attacked mechanistic materialism, citing Haeckel as one of its proponents.

astrophysics and geology. This is perhaps where the main difference lies between Haeckel and Oparin: The latter painstakingly took into account as many factors as possible, relating both to the inherent properties of matter and the external conditions under which the relevant processes could have taken place. Haeckel, on the other hand, was not concerned with the origin of life alone but, without paying too much attention to detail, devised a grand scheme of cosmic evolution. It remains to be seen whether a deeper methodological difference underlies the contrast between the two approaches.

It should be noted that Oparin's criticisms were not primarily concerned with the details of Haeckel's theory but with his mechanistic methodology. The methodological issue at stake, however, is not immediately clear, especially in view of the vast discrepancy in scientific content between Oparin's and Haeckel's theories of the origin of life. It seemed of interest, therefore, to examine some earlier writings on the relation of mechanistic and dialectical materialism to natural science. The first to confront this question was Friedrich Engels (1820-1895) whose writings form a good starting point from several points of view. Firstly, Engels' writings on natural science were contemporaneous with most of Haeckel's works, so that the problem of anachronism does not arise. Secondly, Engels was familiar with many of Haeckel's writings and commented on certain points raised therein. Thirdly, Engels himself was interested in and wrote several passages on the subject of the nature and origin of life, so that a comparison of Haeckel's views and those of a contemporary dialectical materialist can be made.

The basic assumptions of materialism and the historical background of dialectical materialism were treated by Engels in his essay Ludwig Feuerbach and the End of Classical German Philosophy (84), which also includes some remarks on the relation of materialism to science. The latter subject was explored much more extensively by Engels in his Anti-Dühring (85) and in Dialectics of Nature (86), a collection of fragments (some still in note form) written between 1873 and 1886, but not published until the mid-1920s.

According to Engels, the basic question of all philosophy concerned the relation between thinking and being (87). Two opposing doctrines had been in conflict on this point throughout the history of philosophy, namely idealism and materialism. Idealism postulates the primacy of spirit over matter and holds that the external world consists of a set of ideas in our minds, while materialism regards matter as primary and maintains the existence of the external world independent of human consciousness. For the materialist the material, sensuously perceptible world to which we ourselves belong is the sole reality; human consciousness and thinking are the product of a material body, the brain. Matter is not a product of mind according to this view, but mind is the highest product of matter. Moreover, the human mind is capable of reflecting external reality in our ideas and can give us correct knowledge of the world. For example, if we succeed in simulating a natural process artificially (for instance the synthesis of a certain organic compound) then we have proved that our conception of this process was correct and the Kantian "thing-in-itself" (i.e. the organic compound in question) has become a "thing-for-us" (88).

According to Engels, 18th-century materialism was predominantly mechanical, that is to say, it was concerned with the exclusive application of the standards of mechanics to all processes including those of a chemical or biological nature (89). This was its first limitation, explained by the fact that mechanics was the only fully developed science at the time. Its second limitation was its inability to comprehend the universe as a process, as matter undergoing uninterrupted development, rather than a complex of unchangeable things. This tradition was broken with by Marx, who applied Hegel's dialectic to philosophy, but reinterpreted within a materialist framework. Marx saw the world not as a complex of ready-made things but as a complex of processes going through an uninterrupted chain of development (90). From this stand-point, any quest for final solutions and eternal truths became absurd, for all acquired knowledge would be conditioned by the circumstances in which it was acquired. All metaphysical systems would be liable to correction and traditional philosophy was at an end.

Engels distinguished a parallel movement in natural science. Of course, it was necessary first to examine things before it was possible to examine processes; one had to know what a particular thing was before one could observe the changes it was undergoing. Thus, 18th-century science was a science of finished things, a collecting science. And although nature was conceived of as being in constant motion, this motion was seen as an incessant repetition of the same processes, as exemplified by Newton's laws of planetary motion. The first breach in this conception was made by Kant's theory of the nebular origin of celestial bodies, which Engels called the greatest advance in astronomy since the theory of Copernicus (91). Other historical sciences developed in the fields of embryology and geology and culminated in Darwin's theory of evolution. In the 19th century, then, natural science had become mainly a systematising science,

> "...a science of the processes, of the origin and development of these things and of the interconnection which binds all these natural processes into one great whole." (92)

According to Engels these recent developments in science had shown that motion was the basic property of matter; there was no matter without motion and all rest, all equilibrium was relative*. Motion was "the mode of existence" of matter (94). In order to understand matter in motion it was necessary to apply the dialectical method, for

> "Dialectics...comprehends things and their representations in their essential connection, concatenation, motion, origin, and ending." (95)

The dialectic was derived from Hegel, but for the idealist Hegel dialectics constituted the science of the general laws of thought. For dialectical materialism, on the other hand, dialectics is the science of the general laws of motion and development of nature, of human society and of thought. The dialectic of the mind was to be regarded as the reflection of the forms of motion in the real world, both of nature and of history. Hence, the dialectical materialist programme did

*It should be pointed out that, to Engels, motion comprehended all changes and processes in the universe "from mere change of place right up to thinking" (93).

not consist in building the laws of dialectics into nature, but in discovering them in it (96). The three general laws of dialectics were the following:

(1) The transformation of quantity into quality. Quantitative change is at the basis of all qualitative change and at critical stages of development, quantitative change gives rise to qualitative change (97). For example, the members of the paraffin series differ simply in the numbers of carbon, hydrogen and oxygen atoms they contain, but they have very different properties. The transition from one form of motion to another always remains a leap, a decisive change, and the most interesting cases are those where different sciences meet, for example chemistry and biology (98). In the transition from non-life to life, a new form of motion (organic motion) is attained as a result of chemical action and life gains relative autonomy over the inorganic domain.

(2) The law of contradiction or the interpenetration (or unity) of opposites. All change is the result of contradictions in the processes that are undergoing these changes. For example, the association and dissociation of atoms and molecules is the result of opposing forces of attraction and repulsion inherent in the atoms and molecules themselves. To give another example, life is a contradiction, because it is based on the constant self-renewal of the chemical constituents of albuminous bodies necessitated by the opposing forces of absorption and assimilation on the one hand and breakdown and excretion on the other (99).

(3) The law of the negation of the negation. This law is the equivalent of Hegel's law of sublation. Dialectical materialism

itself represented the sublation of Hegel's philosophy and mechanical materialism: both systems were rejected but the progressive elements of each (the Hegelian dialectic and the basic assumptions of materialism) were retained in order to construct a new, superior whole (100).

The dialectical laws are extremely general laws of the development of matter. Engels himself stressed that it is not possible to explain any particular process of development simply by saying that it is a negation of the negation, for instance (101). The same point was emphasised later by Mao Tse-Tung in his essay on contradiction:

> "...we have to study the particularity of contradiction and know the particular essence of individual things before we can adequately know the universality of contradiction and the common essence of things, and ... after knowing the common essence of things, we must go further and study the concrete things that have not yet been thoroughly studied or have only just emerged." (102)

Hence, it was not claimed that the dialectic alone could help us solve any particular problem; it was necessary first to investigate the particular thing or process itself in detail. Granting these limitations, why was the dialectical method regarded to be of such importance to natural science? Engels implied that this was so because dialectical materialism overcame the limitations inherent in other forms of materialism.

Engels criticised mechanical materialism on the grounds, firstly, that it reduced all motion to mechanical motion and, secondly, that it regarded all change as a repetition of processes involving mere change of place of unchangeable entities, instead of processes undergoing continual development.

Hence, Engels criticised the view, put forward in Nature, that mechanics is the statics and dynamics of masses, physics the statics and dynamics of molecules, and chemistry the statics and dynamics of atoms (103). Instead, Engels said that physics is the mechanics of molecules, chemistry the physics of atoms, and biology the chemistry of proteins ("albumens"). Engels believed that this classification expressed adequately how one science passes into another; it expressed both their connection or continuity and their distinction or separation. The classification presented in Nature failed to do this by reducing all sciences to mechanics. Moreover, this reduction was based on the mistaken assumption that mechanical motion exhausts motion as a whole; mistaken, because mechanics deals only with quantitative change while physics, chemistry and especially biology have to deal continually with qualitative change.

It should be noted that Engels' criticisms of mechanism were concerned with the exclusive application of the science of mechanics to problems within the domain of chemistry or biology, and not with the type of reductionist approach which holds that correspondence principles lead from one level of complexity to another, or from one science to another for that matter*. The mechanistic movement in 19th-century biology was concerned primarily with the exclusion of vitalistic and supernatural elements from biology and with the application of a single set

*The same applies to the quite recent criticisms of mechanistic materialism made by Cornforth (104). Cornforth rejects the mechanistic notions that (1) permanent things with fixed properties are the basis of all change; (2) change happens only by the action of some external force; (3) all changes can be reduced to and explained by the mechanical motion of particles; and (4) each particle has its own fixed nature independent of everything else.

of scientific principles to all, including vital, phenomena. In biology, these explanatory principles were largely derived from physics and especially chemistry, where they were well established, but they were by no means confined to the laws of mechanics. Haeckel's monism was mechanistic, but not mechanical in Engels' sense, and it is interesting to note that Engels criticised Haeckel's use of the term "mechanical" but not his methodology in general. He quoted Haeckel as follows:

> "...modern physiology...in its field allows only of the operation of physico-chemical - or in the wider sense, mechanical, forces." (105)*

Engels pointed out that to Haeckel mechanical simply meant non-teleological and that he called every efficient cause a mechanical cause (105). Elsewhere, discussing Haeckel's position on the same point, he commented:

> "With such confusion of language, nonsense is inevitable." (107)

And:

> "Mechanism applied to life is a helpless category, at the most we could speak of chemism, if we do not want to renounce all understanding of names." (108)

These criticisms were not directed against Haeckel's monism itself, nor against Haeckel's approach to biological problems in general or the problem of the origin of life in particular. It will be shown below that, with respect to the latter, there was substantial agreement between Engels and Haeckel.

Besides his criticisms of mechanical materialism, Engels also attacked the "shallow" materialism of scientists such as Karl

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*Italics added by Engels.

Vogt, Ludwig Büchner and Jacob Moleschott who were particularly popular in the 1850s (109). According to Engels, the main occupation of these "vulgar materialists" was the teaching of atheism*, an occupation which he called "not unpraiseworthy if narrow". He took issue with them on two points: Firstly, their abuse directed against philosophy. Engels held that philosophy is necessary to science because facts have to be explained rationally and brought into relation with one another. For example, atoms and molecules cannot be observed under the microscope, but their existence can be deduced by thought. In other words, Engels objected to extreme positivism. Secondly, Engels took issue with the presumption of Büchner and his followers that they could apply the theories about nature to society. To Engels, social processes represented a higher form of the motion of matter over and above biological processes; hence, new regularities not present at the lower level were at work and the social level acquired a certain autonomy over the biological.

The latter criticism could be applied equally well to Haeckel, although Engels did not mention him in this context. Haeckel often reduced social phenomena to the struggle for existence although he rarely went to the same extremes as Büchner, for instance**. In any case, Engels' recommendation to the

*In his Concluding Remarks, Frederick Gregory (see ref.109) also maintains that atheism was the overwhelming trademark of these materialists.

**To give just one of numerous examples that could be cited, Büchner placed excessive emphasis on brain size as a measure of intellectual capacity. On this basis, he claimed that it was firmly established that women were intellectually inferior to men and that the mental inferiority of the (cont. next page) "shallow" materialists that they should study sociology before making any pronouncements on it would not have been amiss in Haeckel's case either. At the same time, this point has no direct bearing on Haeckel's theory of the origin of life and Engels' general remarks on dialectical and other types of materialism do not immediately clarify Oparin's objections to Haeckel's approach to this problem. It remains to be seen now whether Engels' own pronouncements on the subject of the nature and origin of life reveal any basic differences with Haeckel.

In fact, the similarities between the views of Engels and Haeckel regarding life are more immediately obvious than the differences. Like Haeckel, Engels regarded protein as the chemical basis of life. Like Haeckel, he looked upon the transition from non-life to life as a process resulting from chemical action and sought the answer to the problem of the origin of life in the formation of protein. He even accepted Haeckel's view that Monera are totally undifferentiated globules of protein that exhibit the basic phenomena of life (111).

Engels gave the following definition of life:

> "Life is the mode of existence of albuminous bodies, and this mode of existence essentially consists in the constant self-renewal of the chemical constituents of these bodies." (112)

This definition was based on the observation that life had always been found to be associated with an "albuminous body";

(footnote cont.) black race was congenital. He predicted the extermination of the American Indians due to their congenital inferiority. Finally, he illustrated the inferiority of the working class as follows: "It is a daily observation of hatters that the educated classes require on the average much larger hats than the uneducated." (110).

even the lowest known organisms were nothing but simple particles of protein which already exhibited all the essential phenomena of life. To Engels, the most important phenomenon of life was the fact that an "albuminous body" absorbs appropriate substances from its environment and assimilates them while other, older parts of the body disintegrate and are excreted. Non-living bodies may also disintegrate and undergo change, but in doing so they cease to be what they were. The situation is different in the case of living bodies:

> "But what with non-living bodies is the cause of destruction, with albumen is the fundamental condition of existence. From the moment when this uninterrupted metamorphosis of its constituents, this constant alternation of nutrition and excretion, no longer takes place in an albuminous body, the albuminous body itself comes to an end, it decomposes, that is , dies." (113)

Engels pointed out that his definition of life (and, incidentally, of death) was very inadequate in that it did not include all the phenomena of life, but only those that are most common and simplest. In order to gain a complete understanding of life, one would have to understand all the forms in which it appears, from the simplest to the most complex. In addition, it should be pointed out that Engels placed much greater emphasis on what he called the contradiction of life than Haeckel did, i.e. he stressed the dialectical nature of life, arguing that, due to the constant renewal of constituents, life was at any moment itself and yet something else (114). Hence, an organism was no fixed, unchangeable thing but a fluid entity undergoing continual change as a result of its inherent properties and its interaction with its environment.

Life being based on protein, Engels regarded the formation of protein on the prebiotic earth as the crucial step in the processes leading to the origin of life. Because chemists had not yet succeeded in synthesising protein (explained by the fact that nothing was as yet known about protein structure), all that could be said with certainty regarding the origin of life was that it must have been the result of chemical action (115). Engels was confident in asserting this because chemists had already synthesised many compounds that normally only occur in living organisms; not protein, admittedly, but chemistry had gone far enough to assure us that it alone could explain to us the "dialectical transition to the organism" (116). Engels believed that the artificial production of protein would prove the dialectical position in reality; the chemical process would then reach out beyond itself and come into the more comprehensive realm of the organism. (Note that it is assumed here that the synthesis of protein would be virtually equivalent to the synthesis of a living organism.) The dialectical position here was the view that chemical action itself would lead to a transformation of the chemical process into a higher form of the motion of matter, the physiological:

> "Physiology is, of course, the physics and especially the chemistry of the living body, but with that it ceases to be specially chemistry: on the one hand its domain becomes restricted but, on the other hand, inside this domain it becomes raised to a higher power." (117)

Hence, Engels regarded the physiological as a radically new level of development. Physiological processes had a chemical basis but the very confinement of these processes in a coordinated organism led to the development of new chemical processes that could not take place previously. It is important to note that Engels stressed the essential novelty of the living organism as compared with the chemistry of non-living systems. Haeckel, in contrast, always stressed the continuity between the two domains. Engels did not deny that this continuity exists; chemistry, to him, passed into biology. Similarly, Haeckel did not deny that with the formation of protein new processes evolved. At the same time, there is a clear difference in emphasis. Haeckel was mainly concerned with establishing the similarities between living and non-living systems (which ultimately led him to the view that all matter was in some sense alive, as mentioned above) whereas Engels wished to establish in what respects living things differed from and transcended non-living things and to justify the dialectical view that life represents a special form of the motion of matter. Haeckel was still fighting a battle against vitalism, which may explain his stress on continuity, for to do otherwise might have confirmed the vitalists in their opinion that fundamental discontinuities, in particular between the living and the non-living, exist in nature. Engels, however, took continuity for granted and went beyond scientific materialism by advocating a study of the qualitative differences between the two domains, a study of those points where chemistry passes into biology.

There was no conflict between Haeckel and Engels on the question of materialism _per se_; both adopted the basic assumptions of materialism. In fact, Lenin gave a sympathetic account of Haeckel's views for precisely this reason (118).

Lenin was much amused by the furore caused by The Riddle of the Universe (except where this furore turned into violence as when a stone was thrown through the window of Haeckel's study). According to Lenin,

> "There was no abuse not showered on [Haeckel] by the official professors of philosophy." (119)

To Lenin, the irony of it was that Haeckel was attacked for his scientific materialism while Haeckel in his naiveté renounced materialism. Haeckel did not even realise that everything he said was absolutely incompatible with idealism. Lenin criticised Haeckel on one point : Haeckel was a materialist but not a historical materialist; his natural scientific materialism was unable to cope with social problems and had to be broadened into historical materialism. However, in Lenin's opinion Haeckel deserved praise for giving a comprehensive and clear description of scientific progress in the 19th century or, in Lenin's words, of "the triumphant march of natural scientific materialism". Hence, Lenin did not criticise Haeckel for his non-dialectical approach to nature although it should be added that in Materialism and Empirio-criticism Lenin was particularly concerned about the upsurge of idealism in science at the turn of the century (especially in the form of the philosophy of Mach and Ostwald, which had gained a substantial following among certain Marxist groups in Russia). Hence, he defended materialism against idealism but did not explicitly defend the dialectical method in particular at this stage.

Conclusions

Haeckel's monistic philosophy can be criticised on many points, the most important of which are the following:

Firstly, his attempt to avoid a fundamental mind/matter dualism by endowing substance with sensation. This strategy obscures rather than clarifies the relation between mind and matter and could have been avoided by placing more emphasis on the emergence of qualitatively new properties during the historical development of matter, which was after all the basis of his phylogenetic approach. Lodge's criticisms on this point were appropriate, but rather clumsy because he claimed erroneously that Haeckel attributed consciousness to atoms. Engels referred briefly to "Haeckel's bad reproduction of the identity of thinking and being " (120), which probably relates to the same point.

Secondly, Haeckel's tendency to reduce human social history to the biological struggle for existence. It might be added, however, that Haeckel's stress on environmental influences, also in regard to human evolution, made him avoid extreme social Darwinism*.

Thirdly, Haeckel's stress on a purely gradualist evolutionism and his lack of recognition of the emergence of novel regularities during development. All these criticisms are

*Haeckel, however, was hardly the "liberal humanist" he believed he was. His anti-Semitism, his advocation of eugenic measures and, especially in later life, his extreme nationalism have led one historian to conclude that Haeckel's scientific reputation lent respectability to such views and provided a major stimulus to the rise of German national socialism (121).

variations on a single theme: in order to defend his notion of the unity of nature, Haeckel blurred the very real distinctions between different levels of existence, such as the physical, the biological or the social level. The third point, however, is the most relevant one from the point of view of questions of methodology in biology. Lodge defended the autonomy of the living over the non-living but lapsed into vitalism by making this autonomy absolute. To Lodge, the reduction of vital phenomena to, say, physics and chemistry was absolutely impossible in principle. The dialectical materialist position is different because it recognises that each of the "higher" forms of motion (for example life) is necessarily connected with the "lower" forms of the motion of matter, the former having developed from the latter. Hence, reductionism is possible in principle (providing that the historical dimension is taken into account) but at the same time it is argued that a reduction of the complex to the simple fails to provide us with an exhaustive understanding of the special features of the complex, because these differ in quality from the features of the simple. Engels stated

> "One day we shall certainly 'reduce' thought experimentally to molecular and chemical motions in the brain; but does that exhaust the essence of thought?" (122)

Hence Engels' exhortation to the "shallow materialists" that they should study sociology before making pronouncements on it, and hence his interest in those areas where different sciences meet. For example, one should study the laws of society and the laws of biology and then study how the former developed out of the latter. Engels himself made an attempt to do so in his essay <u>The Part Played by Labour in the Transition from Ape to</u>

*Man* (123), where he argued that the biological evolution of the human hand had given rise to labour, which created a radically new set of conditions under which social development according to social laws made a beginning.

An equivalent approach to the problem of the origin of life would be to make a detailed study of the regularities of chemistry (especially the chemistry of carbon compounds) and of biological regularities. Such studies might provide a clue as to how the latter could have arisen from the former. Haeckel did not make such detailed investigations and, in any case, could not have progressed very far considering the state of biochemical knowledge at the time. But Haeckel presented a valid programme, based firmly on his concept of the unity of nature. His notion of substance, with the two attributes of matter and energy, implied that it is the inherent properties of matter that lead to change. His universal law of evolution implied that matter undergoes a process of historical development. And his universal law of causality, which stated that all phenomena in the universe stand in causal connection, implied that environmental influences play a crucial role in the evolution of particular material structures.

These principles seem far removed from the classical mechanistic approach and Oparin's criticisms of Haeckel's methodology appear unnecessarily harsh. Certainly, Haeckel's emphasis on continuity in nature prevented him from seeking explanations in terms of radically new regularities that may have come into being when life began. The concept of a "dialectical leap" in nature would have been alien to him. His materialism was not dialectical, but it was evolutionary materialism of a sort and his writings on the origin of life, however poor in scientific content, should be seen in this light.

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115. *Ibid.*, pp.90,91

116. F.Engels, *Dialectics of Nature*, *op.cit.*, p.249

117. *Ibid.*, p.256

118. V.I.Lenin, *Materialism and Empirio-criticism*, transl. from 1909 edn in Russian, Moscow, 1964, pp.338-345

119. *Ibid.*, p.338

120. F.Engels, *Dialectics of Nature*, *op.cit.*, p.272

121. D.Gasman, *The Scientific Origins of Nationalistic Socialism*, London and New York, 1971

# PART II

## OPARIN'S THEORY, ITS FOUNDATIONS AND ITS IMPACT

## Chapter VII
## OPARIN'S THEORY OF THE ORIGIN OF LIFE

The historical survey presented in Part I of this thesis has shown that, by the 1920s, the problem of the origin of life had reached an impasse. With the ever-growing recognition of the structural and functional complexity of even the simplest living things, it became more and more difficult to account for the origin of the diverse characteristics of living organisms. The literature on the subject remained speculative and little advance was made over the hypotheses formulated in the 19th century. Interest in the subject declined and, with the rise of biochemistry and genetics, attention was concentrated on areas of biological interest that were more easily accessible to empirical investigation. In 1933, Sir Frederick Gowland Hopkins (1861-1947), reviewing the aims and achievements of biochemistry in his Presidential Address to the British Association, expressed a commonly held opinion of the status of the question of the origin of life:

> "Though speculations concerning the origin of life have given intellectual pleasure to many, all that we yet know about it is that we know nothing... Most biologists, I think, having agreed that life's advent was at once the most improbable and the most significant event in the history of the universe, are content for the present to leave the matter there." (1)

Only five years later this situation changed radically, with the publication in English of The Origin of Life (2) by the Soviet biochemist Aleksandr Ivanovich Oparin (1894-1980). This book, first published in Russian in 1936, is generally acknowledged to be a fundamental contribution to the subject, which provided the impetus for subsequent developments in the field. In Part II of this thesis, Oparin's theory and its scientific background will be analysed and an attempt will be made to account for the central position taken by Oparin's theory in the recent history of ideas on the origin of life.

Oparin's first publication on the origin of life appeared in 1924 and was based on a lecture he had delivered to the Moscow Botanical Society. This booklet, entitled Proiskhozdhenie zhizny (The Origin of life) was not published in English translation until 1967, when it was included as an Appendix in J.D. Bernal's book The Origin of Life (3). In 1957, Oparin wrote of this early work:

> "My first work on the origin of life was published as a small booklet in 1924... In it I formulated, though very schematically, the essentials of this problem. I explained these propositions in expanded form ... in 1936." (4)

In other words, Oparin maintained that his views of the subject had not changed fundamentally between 1924 and 1936. An examination of the 1924 booklet therefore seems warranted before Oparin's fully developed theory is discussed.

Oparin 1924: the programme

In the 1924 booklet, Oparin first presented a brief sketch of the notions of spontaneous generation and panspermia. He wrote that the issue of spontaneous generation had been settled conclusively by the work of Pasteur, the concept having been undermined further by later studies that had revealed the complex structure and intricate organisation of microorganisms. The theory of panspermia could only resolve the question of the origin of life on individual planets on the assumption that life had always existed somewhere in the universe, independently from inanimate forms of matter. But this assumption implied that there was an impassable abyss between "the living and the dead"*, a notion which required closer examination in Oparin's opinion.

Oparin's study revealed parallels between all features that were thought to be characteristic of living organisms and phenomena in the non-living world. The chemistry of organisms was not unique, organic compounds obeying the same physicochemical laws as inorganic substances. Similarities in structural organisation, metabolism or assimilation, and self-reproduction were encountered in crystals and colloids. Oparin even noted a phenomenon reminiscent of a struggle for existence in the realm of crystals: depending on the temperature, sulphur crystallises in either octahedral or prismatic form. When the two types of crystal are placed on platinum wires in a supersaturated solution of sulphur in benzene, new prisms are formed next to the prismatic crystals and new octahedra near the octahedral forms. When the two sets of crystals approach each other and come into contact, the prisms are eliminated, the octahedra being "victorious at the first clash" (6). Finally, responsiveness to external stimuli was exhibited by any object with significant potential energy, such as a powder magazine that can be exploded by a single spark. None of these features, then, were unique to living organisms and there was no reason to assume that life was different in principle from the rest of nature:

*Throughout this account, Oparin contrasted the living with the "dead". He would point out later that the term dead should be reserved for things that had previously been alive and that the living was more appropriately contrasted with the non-living (5).

> "Life is not characterised by any special properties but by a definite, specific combination of these properties." (7)

Hence, the most important question concerned the conditions under which formerly disjoint properties could have come together to form the combination characteristic of life. According to Oparin,

> "To discover these conditions would be to explain the origin of life." (8)

The first requirement was to examine the synthesis of organic compounds under natural conditions, taking into account the physical evolution of the earth. Oparin described the latter as seen by contemporary astronomic theory, supported by spectral analysis of celestial bodies at different stages of development, chemical analysis of lava extruded by volcanoes and density calculations of the earth's mass. From the point of view of organic synthesis, the most important stage was reached with the formation, due to cooling, of a solid crust around the liquid core of heavy metals, which included carbon in the form of metal carbides. As a result of further cooling and shrinking, cracks developed in this crust and carbides erupted onto the earth's surface. Thus, carbides came into contact with the atmosphere, in which water vapour was abundant, and formed hydrocarbons, as suggested by experiments in which carbides are treated with superheated steam. In addition, spectral analysis of red stars and comets and chemical analysis of meteorites had revealed a cosmic abundance of hydrocarbons. Hence, the evidence suggested that carbon had first appeared on the earth's surface in the form of hydrocarbons.

Their instability would have led to further transformations, some hydrocarbons being oxidised by oxygen in the atmosphere to give carbon monoxide, carbonic acid, alcohols, aldehydes, etc. The action of superheated steam on nitrogen-metal combinations would have produced ammonia and, subsequently, carbon-nitrogen compounds. Regardless of their exact nature, all these compounds were formed at very high temperatures and consequently had vast reserves of chemical energy, which allowed them to react further and increase their complexity.

Further cooling of the earth's surface led to the precipitation of enormous quantities of water, bringing down organic substances at the same time. From laboratory experiments it could be supposed that the organic compounds in the boiling oceans would have formed substances resembling carbohydrates and proteins. If such substances were formed on earth now they would be consumed immediately by bacteria and moulds, which explained why the abiogenic generation of life was not observed under present conditions (9). In the pre-living world, however, these compounds could undergo many transformations, directed mainly towards aggregation. Hence, ever more complex and ever larger particles were formed and large organic molecules were known to have a tendency to form colloidal solutions in water. The colloidal state being unstable, however, sooner or later gels or coagulates would have precipitated from the solution by chance. According to Oparin, this was a very important step:

> "The moment when the gel was precipitated or the first coagulum formed, marked an extremely important stage in the process of the spontaneous generation of life.

> At this moment material which had formerly been structureless first acquired a structure and the transformation of organic compounds into an organic body took place. Not only this, but at the same time the body became an individual ... With certain reservations we can even consider that first piece of organic slime which came into being on the Earth as being the first organism." (10)

Because of their ability to absorb substances from the surrounding medium, the colloidal gels would grow and eventually break up into smaller fragments by purely mechanical forces, such as surface tension or the breaking of waves. The chemical composition of these particles was changing all the time and each "sister fragment" followed its own course of development. The more efficiently constructed bodies grew faster and the less efficient ones began to lag behind, resulting in a gradual selection of the better organised gels over the very long period during which the processes of chemical change, growth and fragmentation were repeated. This selection led to a slow improvement in the physicochemical structure of the gels, the main result of which would have been an increasingly efficient apparatus for the absorption and assimilation of organic matter from the environment. The energy required for growth and assimilation must have been provided from the break-down of organic compounds. Hence, once the original gels had used up most of the energy inherent in their own constituents, they had to resort to some form of fermentation or respiration to acquire the energy needed for further growth and development. Those that did not acquire any powers of metabolism must have halted in their development and been replaced by bodies capable of breaking down "nutrients".

The absorption of organic substances by the primitive organisms and the break-down of these substances in fermentation or respiration led to a gradual depletion of organic matter in the environment. This marked another important stage:

> "The further life progressed the less nutrient substances were available to the organisms and the more strongly and bitterly the struggle for existence was waged and the stricter and stricter became 'natural selection', rejecting all that was weak and backward and allowing only the most efficient to live."(11)

As they were forced to adapt to these new conditions, the primitive organisms could follow two paths: they could either continue to use the old means of nutrition and eat their "weaker comrades" or they could develop the ability to feed on simple inorganic compounds. Only those organisms which succeeded in taking either of these courses could have survived to evolve further, which suggested that all present-day organisms are ultimately descended from these two types.

No direct evidence in support of this claim was available, but Oparin suggested that a clue was provided by considering the different means of nutrition of present-day organisms. Most bacteria and fungi had been shown to be heterotrophic and also appeared to be the least highly organised among living beings, which suggested to Oparin that the consumption of ready-made organic substances represented the most ancient means of nutrition. The subsequent development of autotrophic feeding did not occur all at once, as revealed by the great variety of modes of metabolism among modern chemosynthetic bacteria: some species obtain their energy by converting hydrogen sulphide into sulphuric acid, others by oxidising ammonia to nitrous or nitric acid and others still by oxidising reduced iron salts. Oparin added,

> "Whether we like it or not, we get the impression that all these various forms of nutrition have been devised because the organisms were forced to find some way out, something which enabled them to exist in the absence of dissolved organic materials." (12)

Oparin pointed out, however, that these chemosynthetic mechanisms are not very efficient and relatively uncommon in the living world. By far the most efficient method of autotrophic metabolism was based on the utilisation of solar energy for the conversion of carbon dioxide into organic matter. As a plant biochemist*, Oparin knew that photosynthesis requires a highly complex physicochemical apparatus which could only have evolved as a result of a long series of transformations within the living cell. He therefore concluded that photosynthesis represents the most recent form of metabolism (13).

This account was followed by a general conclusion in which Oparin stated that his aim had been to show that the origin of life could be explained on the basis of scientifically established facts. In order to develop a more definite theory further facts were required, especially about the properties of colloidal gels and the intricate structure of protoplasm, but Oparin was optimistic that these facts would be forthcoming. Numerous

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*Oparin studied plant physiology and biochemistry at Moscow State University, followed by four years of postgraduate research until 1921. Between 1921 and 1925 he lectured in the Department of Plant Physiology at Moscow. He carried out research on plant proteins and "respiratory pigments" of plants. (Details provided by The Survey of Sources for the History of Biochemistry and Molecular Biology.)

biologists were studying the structure and organisation of living matter and at the same time chemists and physicists were exploring inanimate nature at ever greater depth:

> "Like two parties of workers boring from the two opposite ends of a tunnel, they are working towards the same goal. The work has already gone a long way and very, very soon the last barriers between the living and the dead will crumble under the attack of patient work and powerful scientific thought." (14)

In brief, then, Oparin described a prolonged transformation of organic compounds under the conditions of the prebiotic earth, he attributed a crucial role to the formation and further development of colloidal bodies, and he attached particular importance to evolution at the metabolic level and to the precedence of heterotrophic over autotrophic means of metabolism. Drawing together evidence from different fields of science, Oparin built up a coherent hypothesis which, though lacking in detail, was consistent with contemporary scientific knowledge.

For the time being, Oparin was content to let the matter rest here. He published little on the origin of life* and concentrated on his research into the action of plant enzymes and the mechanisms of plant respiration. In addition, he carried out investigations in such practical areas as the biochemistry of sugar, bread and tea production and helped to organise the Institute of Biochemistry (later named the A.N. Bakh Institute) of the U.S.S.R. Academy of Science, which was founded in 1935 and of which Oparin became Director in 1946. But his interest in the question of the origin

*He published two popular papers on the subject: Die Entstehung des Lebens vom chemischen Standpunkt (The origin of life from a chemical point of view) in Unter dem Banner des Marxismus (1928) and Proiskhozdhenie zhizny na zemle (The origin of life on earth) in Khochu vseh znat (1929).

of life had not waned, as became clear on the publication in 1936 of Vozmoknovenie zhizny na zemle (The origin of life on earth) *, his major work on the subject that would remain his speciality throughout the years.

Oparin 1936: the theory

Compared with the 1924 booklet, the most obvious features of Oparin's work of 1936 are the great detail in which the arguments are presented and the extensive documentation of the scientific evidence, some 230 references being cited. In other respects, the general plan of the two publications followed similar lines: the book starts with an introductory historical section, followed by discussions of the formation and transformation of organic matter on the prebiotic earth, the origin and development of colloidal systems, the origin of primitive organisms and their further evolution as deduced from comparative studies of the metabolism of present-day organisms. The arguments presented will now be examined in detail.

The first three chapters of the book are taken up with a comprehensive historical survey of the problem of the origin of life, starting with Presocratic ideas but concentrating on 19th-century treatments of the problem. This account includes analyses of the relation of these earlier views to vitalism and materialism (15), drawing on discussions of this issue in Engels' Dialectics of Nature (15). Oparin reiterated his previous statements on the concepts of spontaneous generation and panspermia, adding that the latter was now also open to objection on scientific

*Published in English under the title The Origin of Life in 1938.

grounds, after the discovery of cosmic radiation of very short wavelengths that was lethal to all life. Among the theories of a consistently materialistic nature were that of Haeckel and other evolutionists and those derived from artificial cell studies. The limitations imposed by the mechanistic approach adopted in these cases, however, made such theories vulnerable to attack in two ways: first, the transition to life was too abrupt, going directly from inorganic matter to living organisms exhibiting all the basic functions of life*. Hence, all objections to the notion of spontaneous generation regarding the unlikelihood of the sudden genesis of fully adapted organisms applied here also. Secondly, the dependence of these theories on special, unknown environmental conditions or on a particular force meant that no concrete reasons could be given for the fact that life is no longer seen to be arising from non-living matter. According to Oparin, these difficulties could be circumvented by abandoning the mechanistic approach and by adopting the view that

> "... the simplest living organisms originated gradually by a long evolutionary process of organic substance and that they represent merely definite mileposts along the general historic road of evolution of matter." (17)

Such a process could not depend on some unique set of initial conditions or on some simple physical force, but required two conditions: the mass formation of organic substance on earth and a prolonged transformation of this material. These conditions could only be fulfilled on a sterile earth, for if any

*It has been pointed out before that this is an unfair judgement of Haeckel's views. The objection does apply to the work derived from artificial cell studies, such as that of Kuckuck and Butler Burke (see Chapter V of this thesis).

complex organic matter accumulated on earth now it would be devoured rapidly by the countless microorganisms that inhabit the soil, water and air. Hence, there was nothing special about the conditions required for the origin of life, it being generally agreed that the earth was lifeless during its early history. The programme for the rest of the book was then announced by Oparin as follows:

> "To establish the possibility for generation of life in the dim past of the Earth's history, it is necessary first of all to prove the possibility of a primary formation of organic substance on our planet and, secondly, to trace the further evolution of this substance. Contemporary science enables us to furnish a more or less definite answer to both of these problems." (18)

The first step of this programme is dealt with in the fourth and fifth chapters of the book, where Oparin addressed the following three questions. (a) In what form did carbon and nitrogen first appear on earth? (b) What were the conditions on earth when the first carbon and nitrogen compounds appeared on its surface? (c) What transformations did these compounds undergo under the given conditions? A clue to the first question was provided by information on the type of carbon and nitrogen compounds that are associated with stars at different stages of development, other planets in our solar system, comets and meteorites. After a detailed consideration of the evidence obtained by spectroscopy and, in the case of meteorites, chemical and mineralogical analysis, Oparin concluded that carbon was present in the cosmos in the form of elementary carbon, in combination with nitrogen (in the form of CN) and, most of all, in combination with hydrogen (in the form of hydrocarbons).

Particularly striking was the complete absence of any carbon-oxygen combinations, except for the carbon dioxide in the atmosphere of the earth and of Venus. While the carbon dioxide in the earth's atmosphere was clearly of secondary origin, being derived from animal respiration and volcanic eruptions, no ready explanation was available in the case of Venus. The anomaly had to be accepted, although Oparin provisionally favoured a secondary origin of carbon dioxide in this case also.

The study of meteorites was of particular interest to Oparin because they could be analysed directly for their chemical and mineral content and because of the strong evidence for a common origin of meteorites and the earth (19). In meteorites carbon was found mostly in the form of iron carbides, graphite or diamond, cohenite (a carbide of iron, nickel and cobalt) and hydrocarbons. All the evidence presented by Oparin supported his first major claim that

> "... carbon, at least in part, first appeared on the Earth's surface in the reduced form, particularly in the form of hydrocarbons." (20)

Evidence of a similar nature led him to a second conclusion, namely that nitrogen also had first appeared on the earth's surface in the reduced state, in the form of ammonia (21).

With regard to the conditions on earth during its early history, Oparin took as his starting-point the then widely accepted theory of Jeans on the origin of our planetary system. From Oparin's point of view, the most relevant aspect of this theory was the assertion that the planets of the solar system, including the earth, were originally formed from substances making up the solar atmosphere. On this assumption, spectral studies of the solar atmosphere supplemented with geochemical data and chemical analysis of meteorites should furnish evidence concerning the state of the primaeval earth. After discussing this evidence, Oparin presented the following picture of the early earth: a molten core of metals, surrounded by a thin crust of igneous rock and an atmosphere of superheated steam, some nitrogen and other heavier gases. The atmosphere did not contain any free oxygen (if it did, it would be unique among celestial bodies), nor any $CO_2$ and $NO_2$, as it does at present. These gases in the modern atmosphere were of secondary origin, oxygen being derived from photosynthesis and $CO_2$ and $NO_2$ from animal respiration and, in the case of $CO_2$, from volcanic activity.

According to this picture, carbon was present in the form of metal carbides (mostly iron carbides) in the central core of the earth. Eruptions of the molten mass through cracks in the thin and unstable rocky layer would have brought carbides in contact with superheated steam, and it had been known since the 1870s that under such conditions hydrocarbons are formed according to the following reaction scheme:

$$3Fe_mC_n + 4mH_2O \longrightarrow mFe_3O_4 + C_{3n}H_{8m} \qquad (22)$$

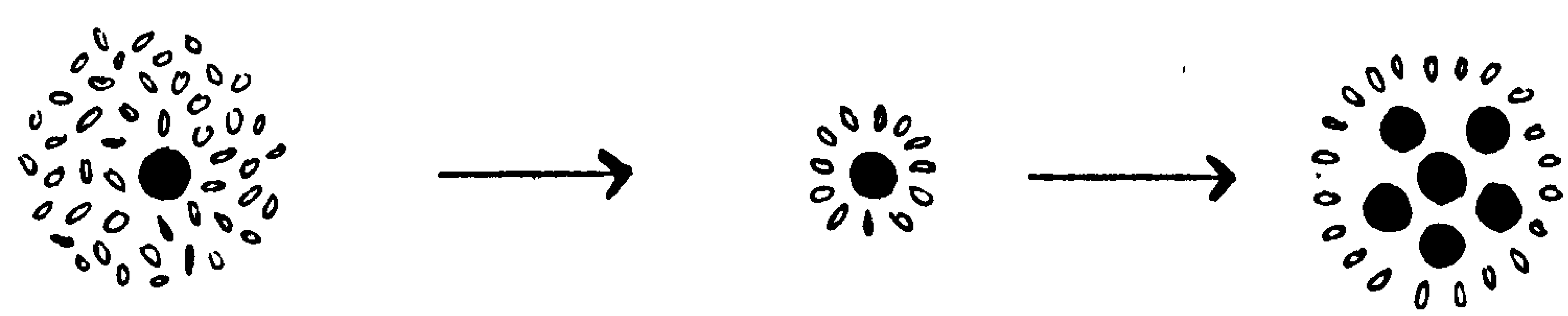
In conclusion, the conditions on the earth's surface during the period under consideration were very different from those prevailing now. The temperature was much higher, the atmosphere was a reducing one and light radiation was more intense. These conditions, however, could be reproduced in the laboratory and the general trend of behaviour of the primary carbon compounds under such conditions could be studied. Using established organic chemical reaction schemes, Oparin concluded that CH and $CH_2$ radicals in the primitive atmosphere reacted with water vapour to form large amounts of unsaturated hydrocarbons, alcohols, aldehydes, ketones and organic acids and that these reacted with ammonia to give amines, amides and ammonium salts (23). As the earth's temperature decreased, oceans were formed and torrential rains brought down the carbon and nitrogen compounds, which continued to react in the aqueous environment, thus forming more complex organic molecules.

In order to get an idea of how, among the immense variety of possible reactions, organic substances relevant to life might have formed in the primaeval oceans, Oparin considered the methods by which these molecules are formed in the living cell. Contemporary biochemistry suggested that three basic types of reaction are involved in living processes: condensation, polymerisation and oxidation (and the reverse processes). In the cell, these reactions had reached a high degree of efficiency through the action of organic catalysts, or enzymes. Because catalysts can only increase the rate of a reaction, but never initiate a thermodynamically impossible process, it could be assumed that all organic constituents necessary for the development of life would also have formed very slowly in the absence of enzymes, though possibly aided by inorganic catalysts, in the primitive oceans. Nevertheless, the formation of these constituents alone could not explain the origin of life. Attempts to deduce the specific properties of life from the atomic configuration of organic molecules were "predestined to failure":

> "The laws of organic chemistry cannot account for those phenomena of a higher order which are encountered in the study of living cells." (24)

In particular, it would be a mistake to look at the properties of single molecules; one should study the interactions between different molecules and study mixtures rather than pure solutions of an organic substance. On mixing, new properties appear that were absent from the components parts. As in 1924, Oparin again emphasised the importance of colloidal systems, which are formed readily by organic compounds of high molecular weight in aqueous solution. The study of colloids was especially promising to Oparin because protoplasm itself appeared to be made up of different colloidal systems.

A discussion of the general properties, the origin and the evolution of colloidal systems is presented in Chapters VI and VII of Oparin's book. With respect to the general properties, Oparin paid particular attention to "hydrophilic colloids" (colloids formed by organic molecules with hydrophilic groups such as -NH, -OH and =O). Besides coagulation, in which colloidal particles run together to form a flocculent precipitate, hydrophilic colloids exhibited another phenomenon of separation, namely "unscrambling". In this case, the colloidal solution separates into a fluid sediment rich in colloidal substance and a liquid layer free of colloids. This phenomenon had been studied extensively by the Dutch chemist Bungenberg de Jong, who coined the term "coacervation" for the process (25). Unlike the coagulate, the coacervate is a fluid mass that is not necessarily continuous but may remain in the form of microscopic droplets floating in the equilibrium liquid. Hence, the formation of coacervates was associated with the appearance of a definite delimitation. In coacervation, the degree of hydration of colloidal particles decreases and only those water molecules that are firmly adsorbed to the hydrophilic groups are retained. Hence, the particles become surrounded by a shell of orientated water molecules, separate from the randomly orientated water molecules of the medium. The process may be pictured as follows (26):



particle of colloidal solution with diffuse water membrane — decrease in hydration — coacervate particle with hydration shell

Coacervates form most readily upon mixing colloidal solutions of particles with opposite electrical charges and their stability is determined partly by electrostatic, partly by hydration forces. As these are opposing forces, the resulting systems are extremely labile and shifts from equilibrium occur by the smallest change in conditions, such as pH or temperature. For Oparin's purpose, the most interesting properties of complex coacervates were their empirically established capacity to absorb substances from the medium and to undergo secondary transformations in structural organisation (27).

Returning to prebiotic times, Oparin concluded that the formation of complex coacervates on the primitive earth was inevitable because the process required very simple conditions: a simple mixing of different hydrophilic colloids in the hydrosphere was sufficient. This was an extremely important event in the evolution of organic substance, which for the first time became separated from the solution by a sharp boundary and, to a certain degree, acquired structure and some elementary organisation. Oparin added:

> "Thus, in coazervates* the behaviour is subject not only to the simplest laws of organic chemistry but also to the newly superimposed colloid-chemical order. However, even this higher order of relationship is still insufficient to secure the origin of primary living things. To initiate life, it was necessary for coazervates and similar colloidal systems to acquire, in the course of their evolution, properties of a yet higher order, properties subject to biological laws." (28)

This is where the capacity of coacervates toabsorb organic substance and to undergo structural transformation entered the picture. Coacervate droplets exhibited a certain degree of individuality and their fate depended not only on external conditions but on their own specific structure or organisation. Only those coacervates in which assimilation predominated over degradation of organic substance could grow and play a role in the further evolution of organic matter. Hence, variations in growth velocity led to a competition between different coacervates

*This unusual spelling of the word coacervates is used throughout the English translation of the book and was probably based on the German Koazervaten.

and resulted in a preponderance of those systems that were best adapted to the external conditions and possessed the most efficient internal organisation. The further the growth of colloidal bodies progressed, the less free organic matter remained dissolved in the earth's hydrosphere so that "natural selection" would have become more exacting:

> "A straight struggle for existence displaces more and more the competition in growth velocity. A strictly biological factor now comes into play. This new factor naturally raised the colloidal systems to a more advanced stage of evolution ... Thus systems of a still higher order, the simplest primary organisms, have emerged." (29)

Finally, then, life arose. Oparin did not stop at this point, however, but went on to examine if a study of contemporary organisms could throw any light on the physicochemical organisation and further evolution of the earliest living beings. The final chapter of his book presents a detailed treatment of this question.

According to Oparin's theory, the earliest organisms could survive and grow only by virtue of absorption and assimilation of organic substance dissolved in the environment. Hence:

> "The organization or inner chemical apparatus permitting assimilation of these substances must have existed, therefore, from the very moment these primary organisms came into existence. This must have inhered in the very foundation of their structure and consequently organisms living at the present time must still be endowed with that apparatus." (30)

This conclusion gained support from the observation that the ability to use organic matter as nutrient was found in absolutely all living things, even those that are now adapted to autotrophic metabolism. Oparin presented evidence that typically autotrophic organisms have retained to a considerable degree the ability to metabolise preformed organic substances. For example, it had been shown that various species of autotrophic algae flourish when nourished artificially with organic substances; they may even become saprophytic and "switch off" $CO_2$ assimilation altogether. Hence, it would appear that autotrophic means of metabolism were superimposed on the more primitive heterotrophic systems. According to Oparin, it would be much harder to explain a loss or regression of originally autotrophic metabolism, none of the present heterotrophic species showing any rudiments of autotrophic processes. Hence, comparative biochemistry supported the view that the original organisms were heterotrophic.

Most synthetic metabolic reactions are endothermic, that is, they require energy. In heterotrophic organisms this energy is obtained from absorbed organic nutrients rich in potential energy. The most efficient way of utilising this potential energy is by complete degradation by means of oxidation reactions. Free oxygen, the most powerful oxidant, was absent from the primitive atmosphere, however, and could not be used for this purpose. Here again comparative biochemistry provided a clue:

> "Many investigations of recent years show unmistakably that the reaction of organic substances by the hydroxyl of water is without exception the basis of all types of energy metabolism of various living things. The only difference between them ... is in the methods of hydrogen acceptance." (31)

Fundamentally, these processes involved anaerobic transformations of organic matter and aerobic respiration again appeared to be a supplementary superstructure, operating only at later stages in the chain of reactions. In addition, it was known to be possible to suppress the aerobic phase to a certain extent and to force higher organisms, at least for a short time, to revert to anaerobic methods, as illustrated for example by lactic acid fermentation in muscle. These data were used to support Oparin's major conclusion that the first organisms were anaerobic heterotrophs:

> "The primitive metabolism of energy was entirely anaerobic and depended on the interaction of organic substances with molecules of water." (32)

Gradually, the supply of organic substances that could be utilised in fermentation must have diminished, being replaced by fermentation products such as carbon dioxide, alcohol, lactic and butyric acid. Eventually a lack of nutrient material would have led to the death of all primitive organisms. In the meantime, however, some organisms must have developed the ability to use light energy for their synthetic processes. Among present-day pigmented bacteria there are some that are strictly heterotrophic but whose ability to utilise organic substance is greatly improved by light. Moreover, the photochemical reactions of such pigmented bacteria which feed on organic substance (and are unable to assimilate $CO_2$) release oxygen by the action of the enzyme catalase, which splits hydrogen peroxide into water and $O_2$. If the ancestors of these bacteria evolved at the stage when organic nutrient was becoming scarce, the conditions for three paths of development would have been created. First, the evolution of a mechanism for freeing oxygen led to the development of oxidative fermentation so that what were previously end-products of fermentation, such as butyric acid, could now be broken down further by oxidation (33). Secondly, organic matter still being scarce and inorganic sources of energy being abundant, some organisms developed chemoautotrophic (or chemosynthetic) means of metabolism in which various inorganic salts are oxidised by means of oxygen. These organisms ultimately evolved into the present-day iron, sulphur and nitrifying bacteria (34). Thirdly, over a long period of evolution, pigmented organisms must have developed the power of photosynthesis, that is, the ability to synthesise organic material from carbon dioxide that had been released by fermentation processes, using sunlight as a source of energy (35).

The origin of photosynthesis marked an important step and radically changed the previously existing relationships. The release into the atmosphere of considerable amounts of free $O_2$, liberated from assimilated carbon dioxide, enabled heterotrophic organisms to "rationalise" their energy metabolism:

> "Speaking broadly, this consisted in the oxidation by atmospheric oxygen of hydrogen resulting from the hydrolytic oxidation of organic substances. In this way the archaic apparatus of fermentation was fully preserved but new physico-chemical structures were added to it, enabling organisms to utilize more fully the chemical energy of nutritive substances." (36)

In other words, conditions were ripe for the evolution of aerobic heterotrophic metabolism, or respiration.

Oparin's theory was now complete. As will be shown in the next chapter of this thesis, its main strength was that it was consistent with knowledge in a wide range of scientific disciplines. More detail was filled in subsequently but Oparin's basic approach remained the same in his later writings. But had his approach changed with respect to the contribution he presented in 1924? The main lines of the arguments were the same: both in 1924 and in 1936 Oparin described the formation and a prolonged transformation of organic matter on the prebiotic earth, the formation and development of colloidal bodies in the oceans, and the evolution of metabolic mechanisms, with heterotrophism preceding autotrophism. There were, however, a number of important changes. In 1924 Oparin had not yet arrived at the idea of a reducing atmosphere, a concept which had two significant consequences. First, reducing conditions made it easier to explain how the gradual synthesis of ever larger and more complex organic molecules could have exceeded organic breakdown by slow oxidation. Secondly, the lack of molecular oxygen in the atmosphere enabled Oparin to refine greatly his sequence of the evolution of metabolic mechanisms and in a way which was consistent with knowledge of comparative biochemistry. In 1924 Oparin did not distinguish between aerobic and anaerobic heterotrophic metabolism, nor did he attempt to explain why anaerobic organisms should have evolved at all if oxygen was always freely available*. In 1924 he regarded photosynthesis as the most recent means of nutrition, in 1936 it was aerobic respiration.

*One can only guess that in 1924 Oparin regarded anaerobic metabolism as a later specialisation, evolved in the course of adaptation of bacteria to specific, oxygen-free habitats. Such an assumption would have been contradicted by the biochemical data presented by him in 1936, and subsequently.

One other difference stands out: in 1924 Oparin emphasised the similarities between the living and the non-living while he later placed more stress on the emergence of novel regularities in the evolution of organic matter. The properties of colloids, for example, were not strictly reducible to physico-chemical laws and life could only be said to have begun when specifically biological factors came into play. This change represents a shift in philosophical outlook from a traditional materialistic one to an explicit dialectical materialist one. The philosophical dimensions of this shift will be discussed further in Chapter X of this thesis. Its most significant consequence for the details of Oparin's theory was that in 1924 he set the actual origin of life at an earlier stage, the initial separation of colloidal gels from the aqueous environment being regarded as the crucial step. In his later writings, Oparin insisted that the origin of life coincided with the emergence of specifically biological factors, such as natural selection.

One of the fundamental propositions made by Oparin in 1936, namely that life had originated under anaerobic conditions, had in fact been anticipated by J.B.S. Haldane (1892-1964) in a brief paper printed in the Rationalist Annual in 1929 (37). Haldane's contribution, while it had little impact at the time, is acknowledged today in the commonly used phrase "the Oparin-Haldane hypothesis on the origin of life". The relations between Haldane's paper and Oparin's work therefore warrant some comment.

Haldane's hot, dilute soup

Haldane became interested in the subject of the origin of life as a result of the controversy that raged at the time on the question whether bacteriophages are living entities or not, and this question forms the starting point of his paper. Bacteriophages, or bacterial viruses, had been discovered by Frederik Twort (1877-1950) in 1915 and independently by Felix d'Herelle (1873-1949) in 1917 (38). The same bacteriophage could infect and induce genetic changes in different species of bacteria. On the other hand, they could not reproduce independently, but required a host for this purpose. Already in 1922, the geneticist Hermann Muller (1890-1976) had suggested that bacteriophages bear a close relation to genes (39), and that they might be regarded as "spare parts" that can be fitted into different "machines". But could genes be regarded as fully alive? Haldane thought not, but pointed out that the bacteriophage controversy indicated that there was doubt as to the proper criterion of life and that intermediate forms, such as the bacteriophage perhaps, might exist (40). Keeping the possibility of intermediate forms in mind, Haldane proceeded to speculate on the origin of life, viewed as a prolonged, gradual process of evolution - chemical as well as biological.

First of all, Haldane suggested that the primitive atmosphere probably contained little or no oxygen, because oxygen is now released into the atmosphere by the photosynthetic activity of green plants. Carbon was probably present in the form of carbon dioxide and the action of water constantly formed ammonia from nitrides and nitrogen-containing minerals in the earth's crust.

Because of the absence of oxygen, there would be no ozone layer in the upper atmosphere and ultraviolet light would reach the earth's surface largely unhindered. Baly and his colleagues had demonstrated that the action of ultraviolet light on a mixture of water, carbon dioxide and ammonia results in the synthesis of a wide variety of organic substances, including sugars and amino acids (41)*. Like Oparin, Haldane pointed out that nowadays such substances would be consumed by microorganisms, but on a sterile earth organic matter would have accumululated until the oceans reached the consistency of a "hot, dilute soup". The action of ultraviolet light would promote organic synthesis of more complex molecules, the latter being sufficiently stable in the absence of oxygen not to be broken down.

Haldane did not suggest any specific steps for the development of organisms from this organic mixture, but did consider the early evolution of metabolism once primitive life had come into being. The first organisms must have depended on fermentation, which characterises life in an anaerobic environment. In other words, the first forms of life were anaerobic heterotrophs dependent on the availability of organic nutrients in the environment. As the nutrient broth became depeleted of suitable substrates for fermentation, photosynthesis must have developed, leading eventually to the evolution of the green plants. With the subsequent release of oxygen into the atmosphere, the

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*The first successful artificial synthesis of an amino acid (glycine) from a $H_2O$-$NH_3$-$CO_2$ mixture was achieved by Löb in 1913, using silent electrical discharges as energy source (42). Florkin, incidentally, wrote that Baly's results have now been discredited, after many failed attempts to repeat the experiments (43).

evolution of animals dependent on aerobic respiration became possible. Haldane believed that animals had probably descended from plants, in view of the similarities between chlorophyll and respiratory pigments* (44).

Finally, Haldane considered the molecular asymmetry of the constituents of contemporary living organisms: sugars are invariably present as the D-isomers and proteins are made up of L-amino acids only. Haldane did not explain how these asymmetries might have arisen, but its existence suggested to him that all living things have a common ancestor.

Comparing Haldane's paper with Oparin's books of 1924 and 1936, it is clear that Haldane was the first to publish the idea that life arose in an anaerobic environment** He defined the possible composition of the primitive atmosphere and recognised the role ultraviolet light might have played in the gradual synthesis of organic matter. He also raised the problem of the molecular asymmetry of living materials. By 1936, Oparin, who was not familiar with Haldane's paper at the time, had

*Chlorophyll, cytochromes and the haem group of haemoglobin are all based on the iron-porphyrin ring. Note that Oparin argued for an independent origin of plants (from aerobic heterotrophs) and animals (from primitive autotrophs) on the grounds that no rudimentary autotrophic mechanisms have been encountered in heterotrophic organisms (45). In fact, the similarity between pigments noted by Haldane may reflect the availability of porphyrins in the prebiotic environment. It has been shown that porphyrins are formed upon passing an electric discharge through methane, ammonia and water vapour (46).

**Nevertheless, at a Conference in 1963, Haldane granted the priority on this idea to Oparin - he had not read Oparin's 1924 booklet (47).

covered all these points, and in much greater detail. The primitive atmosphere suggested by Oparin differed from that proposed by Haldane in that Oparin believed that carbon was present in the reduced form (as methane, for example) rather than in the form of carbon dioxide. The difference is not necessarily crucial because it has been shown that abiogenic syntheses of amino acids, etc., proceed successfully in both types of mixtures providing that the overall conditions are reducing (48). However, Oparin's suggestion was stronger in that it was based on comparative astronomic data.

Oparin's book was of course much more detailed and more carefully documented than Haldane's brief paper. Oparin described precise mechanisms of organic synthesis under the proposed prebiotic conditions and, unlike Haldane, stressed the possible role of colloidal phenomena in the generation of primitive organisms. His suggestions for the evolution of metabolic processes were based on an extensive study of comparative biochemistry as well as on a consideration of the prebiotic environment. In addition, Oparin made an attempt to account for the origin of the molecular asymmetry that is encountered in contemporary living organisms. He favoured an environmental force, such as the action of elliptically polarised light, as the factor responsible for asymmetric organic synthesis on the prebiotic earth (49). Much later, with Yang and Lee's demonstration of the non-conservation of parity, Haldane suggested that the molecular asymmetry of living organisms might be related to the fundamental asymmetry of the universe that was indicated by the work of Yang and Lee (50). The problem of the origin of life's asymmetry remains a controversial one and will be discussed further in the final chapter of this thesis.

Although Haldane's ideas on the origin of life were well known among biochemists in Britain at the time (51), his contribution had no immediate impact on the development of the field. It was only after Oparin's work had provided a fresh impetus to the subject that the value of Haldane's paper was recognised. Haldane remained interested in the problem of the origin of life and wrote a few more papers on the subject (52). However, in view of the great number of fields in which he made significant contributions and in view of his very varied interests, which ranged from enzyme kinetics to the evolution of breast feeding, it is perhaps not surprising that Haldane was never the prime mover of developments in the field of the origin of life.

In contrast, Oparin's book did directly influence progress in the investigation of the problem of the origin of life.

<u>Early theoretical developments after Oparin</u>

The full impact of Oparin's contribution was not felt until 1953, when Stanley Miller reported the formation of significant amounts of amino acids from a gaseous mixture of ammonia, methane, hydrogen and water vapour circulating past an electrical discharge (53). Miller performed these experiments in an attempt to test Oparin's hypothesis of organic synthesis under simulated prebiotic conditions and the success of the experiments stimulated a great deal of further experimental work as well as a great deal of serious interest in the problem of the origin of life.

Before this experimental phase, the problem had received some, but rather little, interest. During the second world war scientists were, on the whole, preoccupied with more pressing problems than that of the origin of life. Nevertheless, a number of interesting theoretical contributions were made in the 1940s. For example, in 1945 Norman Horowitz (born 1915) proposed the means whereby complex biosynthetic pathways might have evolved (54). He based this hypothesis on Oparin's concept of chemical evolution, and its implication that life arose in a complex chemical environment, and on Oparin's idea that the first organisms were completely heterotrophic, maintaining and reproducing themselves at the expense of prefabricated organic molecules in the environment. According to Horowitz, it was not immediately obvious how the long chain reactions characterising most contemporary biosynthetic pathways could have evolved in a step-wise manner from such simple beginnings. For example, two of the intermediates in the synthesis of arginine by the mould Neurospora are ornithine and citrulline, neither of which appear to have any functional significance in the organism except as precursors. Why should the capacity to synthesise ornithine have been preserved by natural selection in these organisms if this could not possibly have conferred any selective advantage on them before the evolution of the complete reaction chain? Horowitz suggested that the problem should be approached in the reverse manner. Consider an environment containing, among others, the compounds A, B and C and an organism that utilises A. As compound A is depleted, organisms that have evolved the capacity to carry out the reaction $B+C \rightarrow A$ (with the aid of a catalyst) would have a selective advantage. Later, compound B might become limiting and organisms capable of carrying out the reactions $D+E \rightarrow B$ and $B+C \rightarrow A$ might evolve, and so on. In other words, the ability to synthesise the precursor B would be more recent than the capacity to synthesise the functional end-product A, in which case the fact that the sole function of B might be its role as a precursor of A poses no evolutionary problem. This ingenious idea was later adopted by Oparin (55).

Another interesting suggestion was made by J.D.Bernal (1901-1971), who made important contributions to molecular biology with his crystallographic studies of proteins and other macromolecules. Bernal discussed the problem of the origin of life in a lecture to the Physical Society in 1947, which was published as a booklet in 1951 (56). In this lecture, entitled The Physical Basis of Life, Bernal followed in the footsteps of Oparin and Haldane, to both of whom he acknowledged his debt. He argued for a materialistic approach to the problem of the origin of life, for the concept of a prolonged chemical evolution prior to the development of life and for a consideration of the evolution of metabolic processes. In addition, Bernal discussed a problem concerning the synthesis under prebiotic conditions of large and complex molecules such as polymers. According to Bernal, the appropriate condensation and dehydrogenation reactions could only have taken place in concentrated organic solutions and not in the extremely dilute state of the oceans. For chemical evolution to have proceeded effectively, therefore, a large-scale concentration of organic solutions must have occurred. One method of concentration would take place in pools and lagoons fringing the coastlines. More favourable conditions for concentration, however, would have been provided by the adsorption of organic molecules to fine clay deposits (57). Clay particles have a very effective adsorptive surface and it had been demonstrated that a wide range of organic molecules are preferentially adsorbed on such surfaces in a regular way, thus promoting the possibility of polymerisation and other chemical transformations. In fact, clays were used as industrial catalysts. Any macro-molecules formed on the surface of clays might subsequently be able to persist independently in colloidal form

Another material on which adsorption could take place was quartz, especially in the form of sand, separately or in association with clays. The importance of quartz was that it is the only common mineral with an asymmetric structure, some crystals having a right-hand twist and others a left. To Bernal it seemed plausible that the molecules that make up living systems had been given a particular twist by the preferential adsorption of asymmetric organic molecules on quartz. Once a preponderance of one particular isomer was produced, even locally, this would lead to conditions where eventually only one kind could be formed*.

In conclusion, Bernal described another step in the process of chemical evolution, in between straightforward organic synthesis

*It has been reported recently that certain colloidal clays (bentonite clays) also bind amino acids and sugars in a stereo-specific manner (58). The binding of the amino acids L-leucine and L-aspartate and the sugar D-glucose to bentonite showed high affinity while there was a less efficient binding of the biologically uncommon isomers of these compounds.

and the formation of colloidal bodies such as coacervates*, a step which had the additional advantage of providing a possible explanation for the asymmetry of life.

The contributions of Bernal and Horowitz are witness to the fact that Oparin's work was indeed "stimulating", as reviewers of his book had written (60). Their suggestions were built on the edifice that had been constructed by Oparin. The foundations of this edifice will now be examined.

*This particular sequence was not made explicit in the lecture, where no specific mention of coacervates was made, but was presented as such by Bernal in 1957 (59).

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# CHAPTER VIII

## THE BIOCHEMICAL BACKGROUND OF OPARIN'S THEORY

As indicated in the previous chapter, Oparin's theory was based on knowledge established in a wide range of scientific disciplines. The physical sciences, including astrophysics and geology, provided information on the likely conditions of the earth in the early stages of geological history. Chemists had accumulated a wealth of knowledge of the properties of carbon compounds; the type of reactions that would have taken place under the suggested conditions could be deduced and a picture of the chemistry of the prebiotic earth's surface and atmosphere built up. A thorough study of established knowledge in these fields provided Oparin with a sound basis for his conclusions that, before the origin of life on earth, the atmosphere contained little or no free oxygen and conditions were appropriate for a wide-spread accumulation of organic compounds on the earth's surface.

The presence of carbon compounds on the prebiotic earth had been postulated previously by 19th-century evolutionists such as Ernst Haeckel (see Chapter II of this thesis). This theoretical feature, however, was presented as a necessary postulate, essential for a naturalistic explanation of the origin of life. Few serious attempts were made to investigate the scientific plausibility of this postulate, the most notable exception being Pflüger's cyanogen theory. It also took many years before the question of the origin of life was treated in relation to specific changes in the environment during the course of geological history. The composition of the atmosphere before and after life appeared on earth was first discussed around the turn of the century. On the basis of an analysis of gases condensed in cavities of rocks, Lord Kelvin concluded that there was no free oxygen in the primitive atmosphere of the earth (1). He suggested that atmospheric oxygen had been released into the atmosphere as a result of the assimilation of carbon dioxide by organisms living in hot springs. Arrhenius also believed, on the basis of comparisons with meteorites, comets and the sun, that oxygen must have been absent from the early earth's atmosphere (2). Neither Kelvin nor Arrhenius, however, discussed the relevance of these suggestions to organic synthesis on the prebiotic earth, presumably because they were committed to the theory of panspermia. F.J. Allen regarded the carbon dioxide and nitrogen as well as the oxygen in the present atmosphere as a product of life, but did not present a clear picture of the composition of the atmosphere before the advent of life (3). A more detailed account of the conditions that would have favoured organic synthesis on the prebiotic earth was presented by the geologist T.C. Chamberlin (1843-1928) and his son (4). The Chamberlins suggested that the early atmosphere would have included the compound gases of carbon, nitrogen, sulphur and phosphorus, but also oxygen (5). On the surface, these elements would have existed in the form of carbides, nitrides, sulphides and phosphides, which reacted to form many combinations, including hydrocarbons. These studies were exceptional, however, and Oparin's stress on historical change in the environment as a whole and on the complex interaction between numerous environmental factors (physical, chemical, protobiological and biological) contrasted sharply with the simpler approach of the 19th-century evolutionists.

Besides this difference in general approach, Oparin was at a great advantage in that much of the evidence he used to support his views of the early history of the earth was not available to his predecessors. For example, many of the spectroscopic data on the composition of stellar and planetary atmospheres were only obtained in the late 1920s and early 1930s. Henry Norris Russell (1877-1957) established in 1929 that there is an abundance of hydrogen in the solar atmosphere and, by extrapolation, in the atmospheres of other stars (6). Hence, a firm astronomical foundation for the view that conditions on the primitive earth were reducing was lacking before 1929*. The discrepancy in factual material available to Oparin and his predecessors was even more pronounced for the next stages in Oparin's scheme, which relied heavily on advances made this century in the fields of colloid science and biochemistry.

Colloid chemists had studied the tendency of organic compounds to form colloidal aggregates in aqueous solution. The work of Bungenberg de Jong in the early 1930s had established that one class of colloids, the individual corpuscles which

*Oparin himself has stated that his views on prebiotic organic synthesis were inspired by Mendeleev's hypothesis of the abiogenic origin of oil and that he was also greatly stimulated by the discovery in the 1930s of methane as a major constituent of the atmospheres of the large planets (7).

he called coacervates, can absorb and assimilate substances from the surrounding medium. Bungenberg de Jong himself had investigated the possible role of coacervation phenomena in the living cell and presented a model of the cell on the basis of his studies of lecithin/triglyceride complexes (8). In particular, the permeability properties of the colloidal films surrounding these "complex coacervates" suggested a model for the "outer border of protoplasm" (9) - a model that subsequently proved fruitful in the study of biological membranes*.

The coacervate concept provided Oparin with a possible scenario for the transition from a diffuse medium containing significant amounts of organic compounds to the formation of individual colloidal bodies capable of developing into increasingly complex structures, probably with the aid of inorganic catalysts taken up from the medium. The fact that both the ease of formation of coacervates and their liability to change by interaction with the environment had been demonstrated experimentally made this a promising approach, although many details remained (and still remain) to be worked out.

So far, then, Oparin's theory was consistent with contemporary scientific knowledge. Nevertheless, there is a significant gap between even the complex coacervates studied by Bungenberg de Jong and the simplest independent organisms known today, the bacteria and the blue-green algae. How could the ancestors of the latter organisms have arisen from

*The relations between coacervates and lipid membranes were discussed by Mitchell at the First International Symposium on the Origin of Life on Earth, in Moscow, 1957 (10). See also Calvin's discussion of the self-assembly of phospholipids (11).

coacervates? No fossils of any "missing links" were available for study* and, had they been available, their dynamic chemical features would not have been open to investigation. This latter point is important because Oparin's theory demanded a functional (bio)chemical link rather than a morphological one. The experiments of Leduc and others, discussed here in Chapter V, had shown that even inorganic colloids could resemble in form a wide variety of organisms, including non-primitive organisms such as mushrooms and higher fungi. Hence, morphological criteria were of little value for the problem at hand. Moreover, a chemical analysis of any fossilised protocells could only, at the best, have provided direct information on the chemical constituents of the intermediate forms, not on their dynamic chemical interactions.

Oparin's approach to the problem was to consider the relations between the known properties of coacervates and the known properties of present-day organisms at a functional chemical level. The most striking feature of coacervates was their ability to absorb substances from the external environment and to utilise the absorbed material in chemical reactions leading to the growth and development of the individual colloidal bodies - a feature strongly reminiscent of metabolism. In general

*The study of Precambrian fossils long remained a controversial subject and early claims of the discovery of an "Eozoon", or organism at the dawn of life, turned out to be baseless - the Eozoon was an inorganic artefact (12). A careful study of fossilised algae was undertaken in the late 1930s in Northern America (13), but very much older fossils have since been found. The oldest Precambrian remains were found recently in stromatolites in N.W. Australia; these appear to be the remains of bacteria and are estimated to be 3.5 billion years old (14). Truly intermediate forms may be older still.

terms, therefore, the phenomenon of metabolism indicated a possible continuity between coacervates and living organisms. In detail, however, the question was more complex. By the start of the 20th century, a great diversity in the patterns of metabolism among microorganisms was recognised. The existence of aerobic, anaerobic, heterotrophic, chemoautotrophic (also called chemosynthetic) and photoautotrophic means of nutrition was well established. Moreover, the relations between microbial metabolism and metabolic patterns in higher organisms were by no means clear at that stage. Under these circumstances it would have been a daunting task to explain the origin of so many different types of metabolism on the basis of chemically very much simpler coacervate models. By the 1930s, however, a unified picture of metabolic mechanisms was emerging and Oparin's choice of metabolism as the fundamental feature of life (a choice already made in his 1922 lecture) could be explored in a fruitful manner. A discussion of the developments leading up to this point therefore seems warranted.

The diversity of microbial metabolism

The great diversity of microbial metabolism came to be recognised as a result of studies of fermentation processes and of chemical transformations performed by soil bacteria. Several historical accounts of developments in these fields are available (15) and here only those advances that turned out to be most important from a retrospective point of view will be summarised.

Although fermentation processes have been used since prehistoric times for the production of bread, beer, wine, vinegar and cheese, the nature of these processes only began to be clarified in the course of the 19th century. Chemical studies by Lavoisier and Gay-Lussac had shown that under the influence of brewer's yeast, sugar is broken down to alcohol (ethanol) and carbon dioxide. The nature of the fermenting agent, the yeast, was, however, a subject of considerable controversy. In 1837, Charles Cagniard-Latour (1777-1859), Theodor Schwann (1810-1882) and Friedrich Kützing (1807-1893) independently demonstrated that the agent of alcoholic fermentation is a living organism. Microscopic observations showed that brewer's yeast consists of globular cells that grow and multiply by budding. These cells were always present when fermentation occurred and fermentation stopped under all conditions which visibly killed the yeast (16). The conclusion that brewer's yeast is a living organism* rather than a chemical substance was not, however, accepted immediately. The great chemist Berzelius (1779-1848), who introduced the concept of catalysis, believed that yeast was a chemical substance that precipitated during fermentation and that the catalytic force of this substance brought about the decomposition of sugar, in a manner similar to the decomposition of hydrogen peroxide upon contact with platinum, for example. Another leading chemist, Justus von Liebig (1803-1873), opposed both these views. He believed that yeast was a decomposition product of albuminous matter and that its

*The organism was called Mycoderma cerevisiae by Cagniard-Latour, and "Zuckerpilz" (sugar fungus) by Schwann and Kützing. The standard name now is Saccharomyces cerevisiae.

decomposition resulted in a "force" of oxidative decomposition being transmitted to the sugar that is broken down during fermentation. Nevertheless, the idea that alcoholic fermentation is caused by a living organism gradually came to be widely accepted over the next two decades*. (Berzelius admitted that yeast is a living organism in the year of his death.) The concept of the participation of living organisms had, however, not yet been generalised to other types of fermentation. In this respect, a major contribution was made by Louis Pasteur and it is with his studies of fermentation that the story of microbial metabolism really began.

In 1856, Pasteur was invited to investigate the repeated failures in the fermentation process used by a manufacturer of industrial alcohol, Monsieur Bigo in Lille. The fermentation of beet sugar frequently resulted, not in ethanol, but in an acid substance smelling of sour milk. Pasteur approached this problem in two ways. First, he subjected the contents of the vats that had failed to produce alcohol to chemical analysis and showed that they contained lactic acid. Secondly, he examined the sediments from the vats microscopically. He found that sediments from vats that had produced alcohol contained

*However, it remained a controversial point whether intact yeast cells are essential for fermentation or whether only "chemical ferments" within the yeast are required. Pasteur adopted the former position and vigorously opposed those who favoured the chemical hypothesis. The matter appeared to be resolved, against Pasteur, when Büchner isolated a cell-free juice from brewer's yeast that performed fermentation in the absence of intact cells in 1897. Büchner believed that he had isolated the enzyme, which he called zymase, that was responsible for the fermentation reaction. It later became clear, however, that Büchner's was a multiple enzyme system, the entire system being required for alcoholic fermentation (17).

large yeast globules, with the buds typical of growth. Sediments from the vats containing lactic acid, on the other hand, revealed the presence of much smaller globules that were in active motion. Upon inoculation of the two types of sediment in a nutrient medium, containing sugar solution and yeast extract, he was able to reproduce alcoholic fermentation with the typical yeast globules and production of lactic acid with the smaller globules. Pasteur concluded that there were two different types of fermentation, producing two different substances (alcohol and lactic acid), resulting from the activities of two different "yeasts"* (18). The importance of this study consisted in Pasteur's recognition that fermentation phenomena are the metabolic activities of specific micro-organisms. Pasteur greatly extended his studies of alcoholic and other types of fermentation, resulting, among other things, in the discovery of anaerobiosis.

In a study of a type of fermentation in which butyric acid is produced (from sugar, mannitol or lactic acid), Pasteur discovered that the fermenting agent was an organism very different from the "yeasts" he had observed before. The organism associated with butyric acid fermentation was cylindrical in shape, straight or curved at one or both ends. The organisms appeared singly or in chains and they tumbled and undulated during movement; they reproduced by simple

*According to Collard, the lactic acid ferment, in this case, was probably <u>Streptococcus lactis</u> (19).

fission. The most interesting characteristic of these "infusoria", however, was their intolerance to even small traces of oxygen. In the absence of any free oxygen, they lived and multiplied indefinitely (given an adequate supply of nutrients). Passing a stream of pure carbon dioxide through the medium did not affect their growth or reproduction. Atmospheric air, however, killed them and as a result butyric acid fermentation stopped (20). This was the first known example of an organism that lives without free oxygen - the first known strictly anaerobic organism.

Pasteur established not only that the fermentation of organic matter depends on the nature of specific microorganisms, but also on the environmental conditions under which the process occurs. For example, yeast cells can live and multiply rapidly in the presence of oxygen but sugar fermentation is very inefficient under these conditions. In the absence of oxygen, however, the yeast does not multiply very rapidly, but on the other hand fermentation is much more active*. The yeast, in other words, is a facultative anaerobe. The term fermentation generally came to be associated with "life without air", characterised by the incomplete breakdown of organic matter, to alcohols and organic acids rather than to carbon dioxide.

An entirely new class of organisms again was discovered in the 1880s and 1890s by the Russian bacteriologist Sergei Winogradsky (1856-1953) - that of the chemoautotrophs.

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*This is the phenomenon known as the Pasteur effect, described by Pasteur in 1872 (21).

Winogradsky was born and grew up in Kiev and, after finishing his schooling at the Gymnasium at the age of 16, entered Kiev University to study law (22). He soon transferred to the Faculty of Physico-Mathematics, but became disillusioned and moved to St. Petersburg to study music at the Conservatorium. In 1887 he entered the natural science faculty of the University of St. Petersburg, where he studied analytical chemistry, attending lectures by Mendeleev and Butlerov, and taking plant physiology as a special subject. He graduated in 1881 and remained in St. Petersburg as a plant physiologist until 1884. He then went to Strassbourg where he was given the opportunity to start his microbiological investigations, "Pasteurian Science" being the field he had become most interested in. His first investigations concerned bacteria found in sulphur- and iron-containing springs and resulted in the discovery of chemoautotrophism.

In a series of papers published in 1887, Winogradsky described his detailed work on the sulphur bacteria (23). Microbes which contained granular sulphur deposits and lived in springs saturated with hydrogen sulphide and containing no free oxygen had already been observed by Cramer in 1870 and by Ferdinand Cohn in 1875. The adaptation of these organisms to such extreme conditions was a matter of great interest and Winogradsky set out to investigate the mechanism and the functional significance of the sulphur deposition in the microbes. First of all, he addressed the question whether the presence of hydrogen sulphide in the environment is the cause or the result of the growth of the organisms. Growing cultures of the red *Beggiatoa* in spring water with $H_2S$ and in spring water containing calcium sulphate, respectively, he observed that sulphur was rapidly deposited by the former culture while existing deposits in the latter disappeared. These and similar experiments led him to the conclusion that *Beggiatoa* can only build up their sulphur from $H_2S$ (24). He further showed that $H_2S$ is absolutely essential for the growth of the organism, that free oxygen plays no part in the oxidation of $H_2S$ to sulphur and that the sulphur is eventually secreted as sulphuric acid. He also demonstrated that the organisms require only minute amounts of organic matter for growth and that they utilise compounds as a carbon source that cannot maintain life in other organisms without chlorophyll, for example formic, butyric and propionic acid. He concluded that the following processes take place: the *Beggiatoa* and other sulphur bacteria oxidise hydrogen sulphide in two steps, first to sulphur and then to sulphuric acid, which is neutralised by reactions with carbonates, especially calcium carbonate, resulting in the production of carbonic acid*. Winogradsky suggested that this oxidation process is equivalent to respiration in the sense that it releases the energy required to the vital processes of the organisms, such as the building up of organic constituents (25). In other words, mineral substances, in this case $H_2S$, play the role of "fermentable

*Which, in fact, serves as the carbon source for organic synthesis.

matter". The actual mechanism of sulphur oxidation remained unclear and Winogradsky did not, for example, discuss the possible role of catalysts in the process. However, his investigations established the existence of a new class of organisms, the Schwefelbacterien, or sulphur bacteria, which differed from other organisms at a fundamental physiological level (26).

Similar studies of rust-coloured organisms such as the Gallionella (the colour resulting from iron oxide deposits) revealed the existence of iron bacteria, which obtain the energy required for growth from the oxidation of ferrous salts to ferric salts (27). Later Winogradsky worked in Zürich, where he investigated the nitrification of the soil from 1899. This work led to the discovery of two groups of organisms, responsible for the formation of nitrites (28) and nitrates (29) from ammonia. These, again, were autotrophic organisms. Finally, Winogradsky isolated the first organism known to be able to fix atmospheric nitrogen; he called it Clostridium pastorianum (later pasteurianum) (30). Extensive studies of nitrogen-fixing bacteria were also carried out by the Dutch microbiologist Martinus Beijerinck (31).

By this time it was clear that bacterial metabolism was extremely varied: heterotrophic organisms required organic substances in the environment for growth; chemoautotrophs utilised mineral substances to obtain the energy required for growth; and photoautotrophs utilised $CO_2$ as a carbon source, the energy for growth being obtained from sunlight, for example the purple bacteria discovered by Theodor Engelmann in the early 1880s (32). In addition, some organisms required the presence of oxygen, others were strictly anaerobic and yet others were facultative anaerobes. At this stage also, only the starting compounds and end products of metabolism and respiration were known; the detailed mechanisms involved in metabolism remained unclear.

This situation changed with the rapid expansion of studies of enzymes and their role in metabolic processes, a trend that was stimulated particularly by Eduard Büchner's (1860-1917) isolation of a cell-free yeast extract that could reproduce alcoholic fermentation (33). Büchner called his preparation zymase, which he believed to be a single enzyme. Already in 1900, however, Carl Neuberg (1887-1956) demonstrated that glucose is not fermented to ethanol in a single step, but in several steps each requiring its own enzyme. Six years later Arthur Harden (1865-1940) and William Young (1878-1942) isolated the glucose diphosphate intermediate that is formed during fermentation (34). Otto Meyerhof (1884-1951) subsequently found that the same intermediate is involved in lactic acid fermentation by muscle, or glycolysis (35). A hint of a possible unity in metabolism emerged and further similarities in different physiological processes became apparent as metabolic pathways were gradually unravelled in greater detail. The first formulation of a unifying principle arose out of a consideration of the role biological oxidations and reductions in metabolism.

The unity of metabolism

A very detailed and well-documented account of the history of the problem of biological oxidations and their role in metabolism is presented by Fruton (36). Valuable histories of cell respiration were also written by Keilin (37) and by Florkin (38). The next two paragraphs will therefore only summarise the main points of interest briefly.

In the 1870s it was established that respiration is an intracellular process, through the work of Traube, Hoppe-Seyler and, especially, Pflüger (39). The nature of the respiratory process, however, was unclear. It was assumed either that oxygen became "activated" in the cell to oxidise organic matter, or that some special property of protoplasmic protein made it reactive to $O_2$*. But another problem remained: what was the role of biological reductions? Such reductions had been known to occur since Pasteur's work on anaerobic fermentations during which hydrogen-rich compounds, such as methane and $H_2S$ were produced. Many proposed that these reductions involved enzymic activation of hydrogen but the role of the process remained obscure.

Further speculations on this matter, and much careful research, gave rise to one of the fiercest debates in the history of biochemistry, that between Otto Warburg (1883-1970) and Heinrich Otto Wieland (1877-1957) after the first world war.

*As has been mentioned before, in Chapter II, Pflüger believed that cyanogen groups of "live proteins" made protoplasm reactive (40).

Warburg made a major contribution to our understanding of the nature and role of respiratory enzymes. His investigations led him to propose that the oxidation of metabolites which characterises intracellular respiration involves the activation of molecular oxygen by a respiratory enzyme ("Atmungsferment"). Wieland, on the other hand, was convinced that the intracellular oxidation of metabolites involves the activation of hydrogen, by the action of "dehydrases" (41). The hydrogen was removed from a hydrogen donor, which was thereby oxidised, and transferred to a hydrogen acceptor, which did not always have to be oxygen. Wieland's work also was very fruitful and led to the characterisation of many enzymes with dehydrogenase activity. The issue remained unresolved until the two theories were reconciled in the oxidation/reduction hypothesis of Kluyver in Delft.

Albert Jan Kluyver (1888-1956) studied chemistry at the Technological University of Delft and supplemented his chemical studies with courses in "microscopical anatomy" under van Iterson (42). From 1910 to 1916 he was an assistant in van Iterson's laboratory and during that period he received a doctoral degree for his research on biochemical sugar determinations. After a period of working in the Dutch East Indies, he was invited to accept the chair of General and Applied Microbiology which became vacant with the retirement of Beijerinck in 1921. In this capacity, Kluyver turned the department in Delft into one of the major centres of microbiology in the world and he is recognised as the main founder of the Delft School of Microbiology. Being an inspiring teacher as well as a great experimentalist and theoretician, Kluyver trained an impressive team of microbiologists who made important contributions to the subject.

Kluyver was deeply interested in the history of his subject and it was this perhaps that made him appreciate the underlying unity of apparently different areas within the field. He brought together a mass of diverse observations in his efforts to establish an underlying unity in microbial metabolism. In 1924, Kluyver presented a lecture entitled "Eenheid en verscheidenheid in de stofwisseling der microben" (Unity and diversity in microbial metabolism) (43). The major part of this lecture was concerned with diversity, but it was suggested already that energetic considerations in the interpretation of biochemical processes might reveal a unifying aspect. Considering that all dissimilatory (catabolic) processes release free energy and that all assimilatory (anabolic) reactions require a supply of free energy, Kluyver concluded that the former reactions represent mechanisms whereby energy is made available to the latter. His speculation that a single underlying mechanism could be involved led him to a clear recognition of the fundamental problem of how energy coupling is brought about. The basic mechanisms of energy coupling were not elucidated until the 1940s and 1950s, when the mechanisms of oxidative phosphorylation, electron transport and photosynthesis began to be clarified at the molecular level; even now rival theories abound and many details remain to be worked out (44).

In 1926, Kluyver published an important paper, together with his assistant Donker, on the unity of biochemistry (45). The authors set out to demonstrate that there is a common chemical basis to oxidative dissimilation and fermentative dissimilation (i.e. anaerobic dissimilation). It was well known that in aerobic respiration oxygen only takes part in the process after the respiratory substrate had undergone an anaerobic transformation, as for example in glycolysis. Kluyver and Donker drew a parallel between the formation of lactic acid in glycolysis and in microbial fermentation of sugars. In all cases they investigated, it was clear that a series of oxidoreductions (coupled dehydrogenation and hydrogenation) was involved and Kluyver and Donker concluded that catalytic hydrogen transfer was the fundamental feature of dissimilatory metabolism. With this concept, a synthesis between the ideas of Warburg and Wieland was achieved

Over the next few years, Kluyver extended his studies of catalytic hydrogen transfer to assimilatory processes and finally reached the conclusion that there is no fundamental distinction between the reactions involved in assimilation and dissimilation: both involve coupled oxidoreductions to release energy from dissimilatory reactions for the use in biosynthetic reactions. In a series of lectures presented in London in 1930, he stated his conclusion as follows:

> "...the whole of biochemistry, the complex of all chemical changes brought about by living cells, can be reduced to chains of voluntary primary reactions, each of which consists in a coupled dehydrogenation and hydrogenation.
>
> Since these oxido-reduction reactions differ in detail, we can summarise the essence of biochemistry in the scheme:

(I) $AH+B \rightarrow A+BH$
(II) $AH.B \rightarrow A.BH$
(III) $AH.B \rightarrow A+BH$
(IV) $AH+B \rightarrow A.BH$ " (46)*

It was in these lectures also that Kluyver coined the phrase "comparative biochemistry" (47), a subject which he believed would become as important for biochemistry as comparative anatomy had been for anatomy. The work of the Delft school certainly bore this out. Kluyver's colleague C.B. van Niel (born 1897) extended the concept of catalytic hydrogen transfer as the basis of metabolism empirically to photosynthesis and chemosynthesis, by his studies of the green and purple sulphur bacteria (49). It was van Niel who derived the general equation of photosynthesis:

$$CO_2 + 2AH_2 \longrightarrow CH_2O + H_2O + 2A \quad (50)$$

In the purple sulphur bacteria, which exhibit a close inter-relationship between photosynthesis and chemosynthesis, the hydrogen donor $AH_2$ was shown to be hydrogen sulphide; in the green plants it was water. Others extended the concept to the methanobacteria (51).

The heuristic value of Kluyver's concept of the unity of metabolism was great, especially in microbiology which had been confronted with so many diverse modes of metabolism. The bacteriologist Patrick Collard has said of Kluyver's concept,

*Eventually it became clear that metabolism involves more than transhydrogenation reactions; transphosphorylation, trans-amination, transsulphuration, transacetylation and trans-methylation reactions were found to play an important role also. Kluyver then noted that all these reactions in essence involve an electron transfer, either between molecules or within molecules. The concept of electron transfer as the basis of energy metabolism led to an even greater unification of views on the mechanisms of metabolism (48).

> "It is seldom in biology that so productive an idea has been brought forward. The only parallels that come to mind are the theory of evolution of Darwin and the concept of the high-energy phosphate bond put forward in the early nineteen-forties by Lipmann and his colleagues." (52)

It is against this background that Oparin's theory of the origin of life, as formulated in 1936, must be seen. He had already adopted a comparative approach and opted for metabolism as the fundamental characteristic of life in 1922, but by 1936 both approaches could be given a much firmer basis. Oparin did not, at this stage, use Kluyver's formulation of the concept of hydrogen transfer, although he did quote van Niel's work on the purple sulphur bacteria (53). Oparin regarded coupled oxidation and reduction as the basis of all metabolism, but believed that these oxidoreductions always involved the splitting of water into hydrogen and hydroxyl groups (54). This view had its roots in the theories of the Russian school of plant physiology in the early 20th century, especially those of A.N. Bakh (1857-1946), S.P. Kostychev (1877-1931) and V.I. Palladin (1859-1922)*. Oparin himself had extended their investigations of biological oxidations and respiratory pigments and had been led to a unified view of biological oxidation and reduction (56). Although Kluyver's formulation of the principle of the unity of metabolism was more general and more fundamental, the search for an underlying unity in both cases was based on concrete findings in biochemistry.

*For a discussion of the contributions of the Russian school of plant physiology, see Florkin (55).

In conclusion, Oparin's view of the fundamental unity of metabolism provided him with a possible link between prevital coacervates and primitive living organisms. At the same time, the diversity of metabolism provided him with a possible sequence of the early evolution of life. This represented a stage of "experimentation", during which the primitive organisms evolved to overcome limitations imposed by the environment and to exploit the environment in many different ways, by the action of natural selection. But the concept of natural selection presupposes the existence of a mechanism of reasonably faithful replication, a subject on which Oparin remained silent in 1936. His silence on the development of a genetic apparatus led him into conflict with those who equated the origin of life with the origin of a gene, a conflict which still has not been fully resolved. Before this controversy can be examined in detail, the background of the genetic approach to the problem of the origin of life must be discussed.

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## CHAPTER IX
## GENETIC THEORIES AND THE CONCEPT OF A LIVING MOLECULE

Oparin's theory of the origin of life provided the main stimulus for subsequent developments in the field. It was not, however, without rivals. In the 1936 formulation of Oparin's theory, biochemical principles played a major role, but genetic concepts were notable for their absence. In the meantime, a different approach to the problem had been developed independently, which had its roots in the theoretical background of genetics. As has been pointed out by Ravin (1), this approach was derived ultimately from attempts to account for a fundamental problem that had confronted students of heredity for a long time, namely the problem that an explanation had to be provided both for the transmission of traits from parents to offspring and for the development of these traits in the maturing offspring. In modern terms, genetic theories must account for gene expression as well as for gene transmission; in more general terms, theories of heredity and theories of development must be consistent. With the rise of Mendelian genetics in the early 20th century, this problem was narrowed down to explaining this dual functional role with regard to the unit factors of heredity proposed by Mendel.

The problem was most pressing to those who regarded the hereditary factors, or genes, as material entities, a view that gained ground as a result of the studies of Thomas Hunt Morgan and his colleagues. Their work on the fruitfly *Drosophila* suggested that genes are tied to a linear structure, the chromosome. Sturtevant's cross-over studies, in which proportions of cross-overs (as revealed by disturbances in the Mendelian ratios) were correlated with the linear distance between different genes, provided strong evidence for the chromosome theory of heredity (2). The recognition of the importance of the relative positions of genes on the chromosome favoured a material concept of the gene. The question was then raised: what type of material structures could both duplicate themselves and determine the development of an organism such that it resembles its parents?

Troland's enzyme theory of life

One of the earliest attempts to answer this question within the context of a material concept of the gene was made by Leonard Thompson Troland (1889-1932). In a paper published in The Monist in 1914 (3), Troland set out to combat the return of vitalism in biology and intended to show that a single physicochemical concept could serve for the rational explanation of those vital phenomena that the neovitalists held to be inexplicable in scientific terms. This was the concept of the enzyme, which would ultimately solve "at least five fundamental mysteries of vital behavior" (4). These mysteries were the origin of living matter; the origin of organic variation; the basis of heredity; the mechanism of individual development; and physiological regulation in mature organisms.

Troland then presented an outline of his solution to these problems, starting with the origin of life. According to mechanistic principles, life must have arisen from non-living matter in the seas of the primitive earth. While protoplasm as we know it would not have come into being in one instantaneous step in Troland's opinion, primitive protoplasm must have had at least some of the characteristic vital properties, namely growth and a certain selective activity with respect to its environment. To Troland, the most likely sequence of events was as follows: the chemical reactions taking place in the primaeval sea would eventually have produced an enzyme by chance. At the same time, colloidal reactions would lead to a slow production of oily substances immiscible with water. If the newly formed enzyme happened to speed up the formation of the oily material, it would eventually become enveloped in this matter. As the oil drops grew, they would be split up into smaller globules by the natural currents of the ocean. The action of the enzyme would stimulate the growth of the oil drops, but repeated subdivision might exhaust the catalyst responsible for the growth process. However, if the enzyme, in addition to its heterocatalytic properties, also catalysed a reaction that produced more of the enzyme itself, then the continued growth of the oil drops, or primitive protoplasm, would be ensured. In brief,

> "...It is only necessary that the enzyme about which [protoplasm] centers should be autocatalytic, as well as effective in the production of primitive protoplasm." (5)

From the idea of the formation of an enzyme with autocatalytic as well as heterocatalytic properties, the solution to the other problems followed: the incorporation of other auto/heterocatalytic enzymes would form the basis of organic variation; the autocatalytic properties of the enzymes would ensure accurate multiplication; and the heterocatalytic properties of the enzymes would be responsible for individual development and physiological regulation. In conclusion,

> "Life, according to our conception, is something which has been built up about the enzyme; it is a corollary of enzyme activity." (6)

Troland admitted that the most serious objection to his idea might concern the fortuitous original formation of the enzyme, which some might regard as a highly improbable event. However, an improbable event was not the same as an impossible event and, according to the theory, it had to take place only once over a period of many millions of years for the process to have started. Under these circumstances, Troland felt that such objections would lose their force and become "almost absurd" (7). In a later paper, where Troland gave his theory the name of "the enzyme theory of life" (8), he suggested that the first enzyme be called protase (9).

Troland's theory was adopted, at least in outline, by the geneticist Hermann Muller who believed that the assumption that genes have auto- as well as heterocatalytic properties would indeed solve a number of fundamental problems in biology and genetics (10). Although Muller was reluctant to equate genes with enzymes, and later scientific developments justified this reluctance, he did retain the idea that the origin of life must be sought in the origin of the gene (11). His views on the origin of life throughout depended on the chance formation of specific molecules with the dual properties (replication and control of developmental and physiological processes) of the gene. Hence, he equated the origin of life with the origin of specific molecules, rather than with the origin of multimolecular, well-coordinated, self-maintaining systems as was the approach of Oparin and his followers. Muller's approach had a great influence on geneticists and, later, molecular biologists. The conflict between the two approaches became particularly evident at the First International Symposium on the Origin of Life, held in Moscow in 1957.

The primacy of the hereditary material and genetic concepts

In fact, this controversy was foreshadowed 45 years earlier, at a meeting of the British Association at Dundee in 1912. One of the sessions was concerned withthe problem of the origin of life and a report of the discussions was presented in *Nature* (12), highlighting the controversial nature of the subject*. Among the points of contention were the validity of a mechanistic approach to the problem (with J.S. Haldane, among others, arguing against the feasibility of a chemico-physical approach), the degree of complexity of hypothetical primitive organisms (the proposals ranging from ultramicroscopic bodies structurally far removed from contemporary cells, to colloidal bodies, and to organisms resembling present-day blue-green algae), and the relative importance of the nucleus and the cytoplasm in the early development of life. The latter question was raised by E.A. Minchin (1866-1915), who opened the discussion.

Minchin argued that the chromatin substance invariably present in cell nuclei represented the primary and essential living matter and that the earliest forms of life were minute particles of chromatin, around which, in the course of evolution, achromatinic (cytoplasmic) substances were formed. Minchin's argument was based on the observations that chromatin is present in the cells of all living organisms, that chromatin always divides first

*The presidential address in 1912 was given by E.A. Schafer, who also dealt with the question of the origin of life (see Ch.II of this thesis). The discussion and the President's address, however, were independent according to the meeting report in *Nature*.

Another Controversy

(It has recently been debated at great length whether the origin of Life is to be found in a primitive substance called Chromatin or in one called Cytoplasm.)

Oh, oft with me you've had it out
Thomas, in many a deadly bout,
Crossed swords at many a juncture;
Pinked me, it may be, with the point
Right through my dialectic joint,
Or felt in turn the puncture

You've fought for Warwick - I for Kent;
You've sworn by Swanage - I have lent
My weight to Tobermory;
I (that a duel might occur)
Have been a Little Englander -
You quite the Little Tory

We've had it out on Art v. Life,
On Rose v. Rachel (as a wife),
On Cook opposed to Peary;
We've argued Commons versus Peers,
Varsity v. the Temple beers,
KHAYYAM v. PETER KEARY.

On Increments and Censorship
(Subjects of which we have no grip
Afford the keenest fighting)
We've said our most excited say,
And argued half a summer's day
MORRISON versus WHITEING

Any old controversial thing
Has done for us to have our fling -
Baconian - Erasmist;
So now, on guard with supple wrist -
You as a strong Chromatinist -
I as a Cytoplasmist

(Reproduced from Punch, Vol.143, 1912, page 245) during reproduction by fission, that chromatin plays an essential role in fertilisation and probably also in heredity, and that nucleated cells cannot continue to live when deprived of their nuclei. In addition, he mentioned a recent finding that the "protein molecules" of the nucleus were, allegedly, simpler in constitution than those of the cytoplasm, suggesting that the former are more primitive.

A lively discussion followed these pronouncements, which received considerable publicity, even in Punch. The poem reproduced opposite appeared in Punch on September 25th, 1912, predating the Dundee meeting report in Nature by well over a month.

Minchin's chromatin theory was an early formulation of the concept of the priority of the hereditary material in the beginnings of life. This concept, which in much refined form became one of the main points of conflict at the Moscow Symposium, went through several stages related to advances in genetics: (1) a stage preceding the wide acceptance of the chromosome theory of heredity; (2) concepts inspired by the chromosomal theory of heredity; (3) a phase in which the "one gene—one enzyme" concept of biochemical genetics played a dominant part; (4) and the most recent stage, inspired by the findings of molecular biology, especially the molecular structure of the nucleic acids and the latter's role in protein synthesis.

Minchin's and Troland's theories clearly belong to the first stage. As mentioned above, Troland identified his autocatalytic enzymes with the Mendelian factors of heredity, but nowhere did he indicate any specific material (let alone any specific chemical structures) that could form the basis of the autocatalytic particles. Minchin based his views not on the complex structure of the chromosome (in fact, he did not mention chromosomes), but on individual particles of chromatin. In a paper based on the opening address he delivered to the Zoological Section of the British Association in Manchester in 1915 (13), Minchin reiterated his view that the first living beings were

> "...minute, possibly ultramicroscopic particles which were of the nature of chromatin." (14)

At the same time, he stressed that he used the term chromatin in a strictly biological (i.e. functional) sense and that chromatin might have changed chemically during the course of evolution. For the original chromatinic "organisms" he used the term "biococci" and he postulatedthat their formation must have been followed rapidly by differentiation. First, the living units would become surrounded by a rigid envelope and develop into the bacterial type of organism. Next the organisms would have become surrounded by a matrix of protoplasm and finally the chromatin grains would have evolved into definite cell nuclei, differentiated from the protoplasm or cytoplasm. Even in contemporary organisms, the chromatin constituents of the cell should be regarded as

> "... a number of minute granules, each representing a primitive independent living individual or biococcus. To each such granule must be attributed the fundamental properties of living organisms in general..." (15)

Minchin refrained from speculating on the mode of origin of the original chromatin particles, because he felt that such speculation would be premature in the absence of detailed knowledge regarding the chemical structure of chromatin.

A third representative of the "living molecule" school who did not explicitly rely on the chromosomal theory of heredity was Charles B. Lipman. In a critical review of various hypotheses on the origin of life published in 1924 (16), he concluded that most theories on the origin of life, apart from the panspermic hypothesis (which begged the question, in his view), postulated that proteins are absolutely essential to life. One type of theory, that of Troland, depended on the chance formation of a single protein with autocatalytic properties. To Lipman this seemed highly improbable in view of the fact that the autocatalytic substance was

> "... so complex a substance that chemists have not succeeded in discovering its nature." (17)

In fact, he thought that if one started by postulating the sudden appearance of an autocatalytic enzyme on the primaeval earth, one might as well postulate that of an amoeba.

The second type of theory postulated the successive formation of simple, then complex chemical substances, and finally protoplasmic substance with the attributes of life. The latter transition was unsatisfactory to Lipman, as it implied a large gap between the non-living and the living. A truly gradual transition could only be conceived if life began in the form of a "living molecule", much simpler than the protein molecule and

> "...in which the behaviour of the substance in regard to motion, growth and reaction with its environment was not, perhaps, the same but, in a primitive way, similar to that of an amoeba, and we would have our first living molecule." (18)

The first living molecules would have arisen out of reactions between carbon dioxide, water and nitrates, and by gradual aggregation they would, over a very long period, have given rise to proteins and protoplasm. Again, the nature of the first living molecules was not discussed in chemical terms and the notion remained very hazy.

With the rise of the chromosome theory of heredity, the concept of an ancestral living molecule, while not immediately gaining in chemical precision, at least came to belong to a more restricted domain, namely that of possible precursors of the chromosomal material having the dual function of self-replication and control over other processes or reactions. In Hermann Muller's earlier writings on this subject, he stressed the functional aspects of the gene and the comparative complexity of the protoplasm. This complexity made the explanation of the primaeval development of protoplasm highly problematic. In addition, wrote Muller, one could not speak of living matter unless this matter had the property of growth, which, in chemical terms, involved autocatalysis (19). Genes being the autocatalytic units *par excellence*, this meant that in the evolution of living matter, there probably never was any protoplasm having the power of growth unless it contained genes, and

> "If this is true, it means that life did not occur before the gene." (20)

Adopting Troland's notion of the original formation of an autocatalytic particle that also had heterocatalytic properties, Muller felt that he could avoid the difficulty of accounting for the origin of present-day protoplasm. The complex protoplasmic system came about gradually, step by step, as mutation followed mutation in the primordial autocatalysing genes and as those mutant genes whose by-products were most useful in further reproduction survived preferentially. In conclusion,

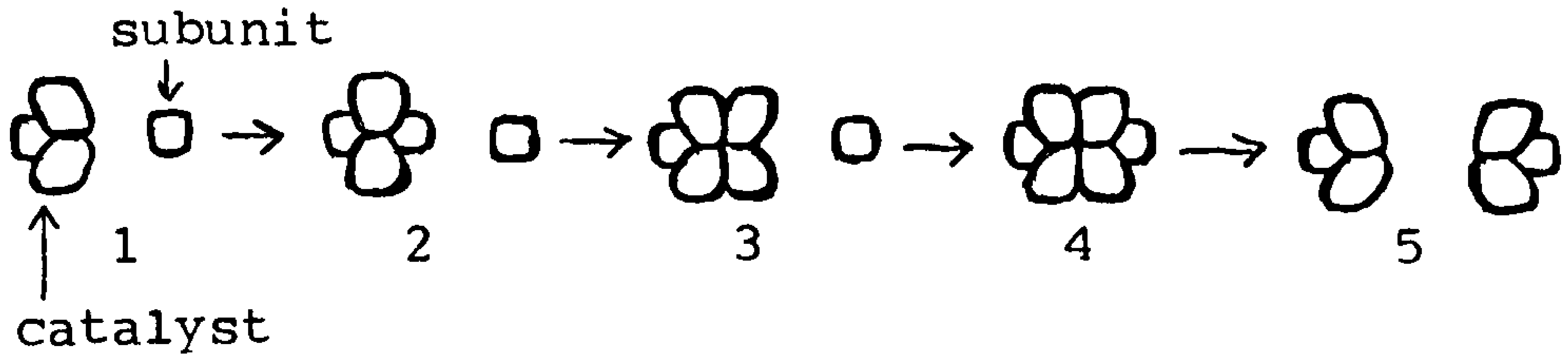
> "On this view, then, the view that seems best to stand the tests of ultimate analysis, the great bulk, at least, of the protoplasm was, after all, only a by-product, originally, of the action of the gene material; its 'function' (its survival value) lies only in its fostering the genes, and the primary secrets common to all life lie further back, in the gene material itself." (21)

Muller did not postulate a chemical mechanism for the first formation of the autocatalytic gene, but indicated that physicochemical studies of chromosomes or viruses, including bacteriophages, might be fruitful in this respect. Later he particularly emphasised the role of chance events in the formation of the first genes by "blind chemical forces" (22). At this stage, Muller's views combined elements of the theories of Troland and Minchin, interpreted in the light of the genetics of the Morgan school.

An attempt to provide some sort of physicochemical explanation for the autocatalytic properties of genes was made by the colloid chemist Jerome Alexander (23). Starting from the concept that genes are subunits of chromosomes, of the dimensions of large molecules, Alexander discussed the auto- and heterocatalytic properties of the gene. The phenomena of gene linkage and crossing-over indicated that each subunit of the chromosome reproduced itself next to itself. In addition, any changes in the subunits had been shown to produce marked changes in the cell and its offspring. Hence, the genetic subunits could be regarded as

> "...specific catalytic particles which direct chemical changes within their respective domains, and thus dominate life processes." (24)

For his attempted physicochemical explanation of the duplication (autocatalysis) of the particles, Alexander resorted to somewhat vague colloidal notions: a catalyst particle composed of several simple molecular subunits also present free in the medium would successively absorb its constituent subunits and then separate itself into two identical particles as follows:




The successive reactions, according to Alexander, depended on changes in the surface charge of the colloidal particle (25). Evidence for the existence of the hypothetical free-living self-reproducing catalytic particles was provided by the ultra-filtrable viruses and bacteriophage, which, in Alexander's opinion, approached such particles in simplicity. With respect to the question of the origin of life, Alexander felt that this theory suggested strongly that the first living thing had been a molecule or simple molecular group exhibiting the directive and self-duplicating power of the gene (26).

Curiously, Alexander's views remained substantially the same for the next 20 years. In a book published in 1948, he continued to stress catalysts as the "ultimate living units" and to endow the genes with the essential catalytic properties he had attributed to them in 1929 (27). By then, however, it was established, through the work of Avery and his colleagues (28), that the nucleic acids formed the basis of the genes, while the catalytic properties of the cell had become firmly associated with specific enzymes of the nature of proteins. The nucleic acids themselves have little or no catalytic activity. It must be assumed, therefore, that Alexander was using the term catalyst in what was by then a very idiosyncratic manner, referring to self-duplication and control of enzyme synthesis. His ideas on the original formation of his "catalytic particles" had not gained any precision either by 1948.

The spontaneous formation of a self-reproducing enzyme was also postulated by Reinhard Beutner, Professor of Pharmacology in Philadelphia, in a book published in 1939 (29). Beutner was particularly impressed with the crystallisation of tobacco mosaic virus, achieved by Wendell Stanley in 1935, which indicated to him that viruses are single molecules. As regards the nature of these molecules, he made the following statement:

> "There is positively no reason to deny that a single molecule has the essential properties of a living organism, if it is an enzyme which has the power of producing in a naturally occurring environment chemical reactions that lead to its own multiplication. This means that such an enzyme propagates itself in the same manner as a living organism. In this sense life is a property of matter, but only of a highly specialised kind of matter." (30)

Such self-reproducing enzymes might have arisen early in the history of the earth, possibly with the aid of electric discharges. The cell, according to Beutner, was a much later development (31).

Beutner's book is of particular interest because he included an Addendum discussing Oparin's theory, which had appeared in print in English shortly after Beutner's manuscript had gone to press. Beutner regarded Oparin's statements on the gradual formation of organic matter on the prebiotic earth as extremely important and discussed them at considerable length. Their relevence to his own enzyme theory was clear:

> "The assumption that sparks can eventually form self-regenerating enzymes would seem to be even more probable if the early earth had plenty of hydrocarbons in its atmosphere." (32)

Hence, Oparin's investigations tended to

> "...supplement and clarify our ideas about the gradual evolution of life from lifeless matter." (33)

However, Beutner noted some important differences between the two theories in the sense that Oparin attached no importance to self-regenerating enzymes or "to any form of life consisting of single molecules" (34). According to Oparin, the first forms of life were much larger: first coacervates were formed, and as enzymes were formed inside them, these coacervates eventually developed into living organisms. According to Beutner, on the other hand, life-producing enzymes appeared first, followed by the building up of a structure around them. In Beutner's view,

> "The entire difference between the two opposing views is therefore only concerned with the order of the essential events which preceded the appearance of life." (35)

As has been pointed out by Loren Graham and by Farley, for example, the point at issue was of a more fundamental nature. The philosophical issues at stake will be discussed in the next chapter. It is necessary first to complete the review of the development of the genetic or "single molecule" approach to the problem of the origin of life.

<u>Biochemical genetics and the protogene</u>

In the 1930s, advances in biochemistry made it possible to study gene function, supplementing previous studies of gene transmission. The genotype and phenotype, which previously had been separated by a "black box", were now seen to be joined by chains of biochemical reactions. Especially the work of George Beadle and Edward Tatum with the mould *Neurospora crassa* suggested the idea that each gene is responsible for the synthesis of one enzyme (36). This concept of a one-to-one correspondence between genes and enzymes involved in biochemical reactions, in fact, formed the starting point for the hypothesis of Horowitz on the evolution of biosynthetic pathways*.

In his sequence towards an ever-increasing independence from ready-made organic molecules in the environment, Horowitz wrote of mutants capable of synthesising more and more intermediates in the chain of reactions leading to the formation of the desired end-product. Denoting the end-product as A and the immediate precursors as B, C, et., he gave the successive mutants the genotypes (B+C→A), (D+E→B, B+C→A), etc. (37). Horowitz assumed, therefore, that the first heterotrophic units were already endowed with a fairly advanced genetic apparatus. In discussing Oparin's theory of a prolonged "chemical evolution", Horowitz also postulated that the "first self-duplicating nucleoprotein" had originated in the course of this process of chemical evolution (38). At this stage, however, Horowitz did not state explicitly that the nucleoprotein material itself was

*See Chapter VII, pages 251,252.

alive (or not), nor that the genetic material was absolutely primary in the development of life. As will be shown in the next chapter, by 1957 his views had become more definite.

Horowitz's scheme was adopted by George Beadle (born 1903), who, however, came out more clearly as a representative of the "living molecule" school (39). After a discussion of Oparin's ideas on chemical evolution, he added:

> "Somehow out of this age-long trial-and-error process there presumably arose molecules with the property of duplicating themselves, that is, capable of catalyzing the process by which they were formed. If such molecules were at the same time sufficiently large and appropriately built to permit chemical modification without loss of power to multiply their kind systematically, they could become the ancestors of further lines of evolution, now definitely organic." (40)

With respect to the properties of self-replication and mutation these molecules probably resembled genes and viruses in so far as they shared similar mechanisms of autosynthesis. Beadle here added candidly,

> "...an assumption that does not help us much, since we know very little about how [genes and viruses] build more of their kind." (41)

According to Beadle, the formation of a self-duplicating mutable molecule, or "protogene", had probably only taken place once; it was a chance event of low probability. His further remarks on the hypothesis of Horowitz did not add substantially to the original formulation, except in so far as Beadle adapted it to explain the successively more complex mode of synthesis of the protogene itself in the process of replication.

Essentially the same account was given by George and Muriel Beadle in 1966, in a popular book on molecular genetics (42): nucleic acids and proteins were formed in the prebiotic soup from simpler building blocks; at some stage a nucleic acid molecule and a protein molecule combined, the protein becoming a protective coat for the nucleic acid. The new nucleoprotein molecule then had to develop the ability to make a protein coat for itself whenever it duplicated, as do present-day viruses; once this had been achieved the nucleoprotein molecule had become a "protogene" (43).

In the meantime Muller had reiterated his earlier views on the origin of the gene as life's essence on a number of occasions. Although his views had not changed substantially, a number of new trends in his writings are relevant to the present discussion. In a Pilgrim Trust lecture (44), delivered in 1945, Muller first dissociated himself explicitly from Troland's concept of an autocatalyst:

> "It has been misleading and unhelpful to refer to the self-duplication of the gene as 'autocatalytic', and Troland's otherwise brilliant papers .... are marred by his insistence on this. For the term is a 'blanket' one, referring merely to the end result.... There are many and totally diverse mechanisms by which such a result is brought about, and an understanding of one of them seldom helps with another." (45)

In the same paper, he referred to Oparin's concept of a long process of chemical evolution antecedent to the origin of life, characterising this concept as "a necessary part of the theory that the gene constitutes the basis of life" (46). He also alleged that those who explicitly or implicitly adopted an "organism-as-a-whole" approach to the question of the origin of life tended to deny the existence of a special genetic material (47). In a paper published in 1955 (48), Muller associated the protoplasmic or "organism-as-a-whole" approach explicitly with the concept that metabolism developed prior to the genetic material, a view he attacked on the grounds that while changes in genes lead to changes in metabolism, the reverse was known not to be the case. In a particularly vitriolic attack on the protoplasmic/metabolic view, he wrote in 1966:

> "It is a curious anachronism, however, that even today some of the most eminent biochemists and biologists, doing very valuable work in their respective fields, still adhere to this view of the primacy of metabolism and its corollary concerning life's origin. Unfortunately, it became much publicized and elaborated, beginning in the 1930's, by the Lysenkoist Oparin in his book The Origin of Life (1938 et seq.), as a part of the attempt to down-rate the significance of genetics. His part of that attempt was most subtly carried out." (49)

Before discussing the basis of this anti-genetic "conspiracy", a few words must be said about the influence of molecular biology on the genetic approach to the origin of life.

DNA and the origin of life

With Watson and Crick's elucidation of the structure of DNA in 1953 (50), a mechanism for the self-replication of the genetic material (by then known to be DNA) was immediately suggested: the two complementary strands of the double helix might separate and new polynucleotide chains be made on the surface of the separated strands by adding pre-existing molecules onto the growing ends of the new chains. The specificity of each newly added nucleotide would be directed solely by the nucleotide on the template chain by virtue of the adenine-thymine and cytosine-guanine complementarity rules. This process was later confirmed and was shown to require the action of a single type of enzyme only, the DNA polymerases (of which the bacterium Escherichia coli has been shown to have at least three).

By the 1950s, it was also clear that different proteins have specific amino acid sequences and it became likely that specific amino acid sequences were somehow determined by specific nucleotide sequences on the DNA molecule. There was, however, evidence against the idea that DNA itself served as a template of protein synthesis: DNA remains almost exclusively within the cell nucleus while protein synthesis had been shown to take place within the cytoplasm and to be associated particularly with the ribosome particles, which are rich in RNA. This suggested that RNA mightbe the templatefor protein synthesis and gave rise to the concept of a genetic code and to the sequence hypothesis which states that DNA determines RNA and RNA determines protein, in that order. The frantic searchfor the genetic code and the mechanism of protein synthesis has been described exhaustively by Horace Judson in his Eighth Day of Creation (51) and only the main points will be summarised here. In the 1960s it was established that the information contained in DNA (in the form of its specific nucleotide sequence) is transcribed according to the nucleotide complementarity rules onto messenger RNA (mRNA), which then moves out of the nucleus into the cytoplasm. Individual "codons" consisting of three nucleotide bases on the mRNA template bind to complementary "anticodons" on transfer RNA (tRNA) molecules bound to amino acids activated by means of ATP. Each tRNA molecule is specific for one of the 20 amino acids that commonly make up proteins, so that the codon-anticodon combination lines up amino acids in a specific sequence. In other words, the nucleotide sequence is translated into a specific amino acid sequence. The process of protein synthesis requires a vast machinery of enzymes, including RNA polymerases and specific aminoacyl transferases.

Before these facts had been discovered, Francis Crick had in 1958 formulated the "central dogma" of molecular biology, which states, briefly, that information transfer from protein to nucleic acid is absolutely excluded (52). The apparent paradox that, in contemporary organisms, the information content of nucleic acids is required for protein synthesis while enzymes, i.e. proteins, are required both for DNA replication and the control of protein synthesis by DNA gave rise to the question of which, in the development of life, had come first, DNA or protein. In addition, the genetic (triplet) code appears to be universal* among all contemporary organisms, which raises the question of how this code arose.

Two prominent workers who have attemptedto investigate the mechanism whereby the nucleic acid-protein relationship arose, possibly from short and simple nucleotide and amino acid sequences, are Francis Crick and Leslie Orgel (53). Both emphasised the importance of studying the stereochemical interactions between nucleic acids and proteins or their precursors. So far, however, this type of study had not (and still has not) produced concrete results that could explain the universality of the genetic code. Crick suggested as an alternative, admittedly less satisfactory, hypothesis that the code is the result of a "frozen accident". Both Crick and Orgel have

*The code, however, appears to be slightly different in mitochondrial DNA (see Chapter XI, page 357).

approached the question from the point of view that functional precursors to contemporary nucleic acids and proteins and their interrelationship arose in the general prebiotic environment, prior to the formation of cell-like structures. Orgel has presented a particularly clear account of this approach in his book The Origins of Life, subtitled Molecules and Natural Selection (54), where he deals with the question of how replicating polymers could have arisen from random, non-informational molecules.

Finally, it ought to be pointed out that the "selfish gene" theories currently in vogue are an extreme expression of the concept of the absolute priority of DNA, not only as far as the origin of life is concerned, but also in the entire subsequent evolution of life (55). The view that all organisms are mere propagating machines to ensure the survival of individual genes is an extension of the concept of "protoplasm as a by-product".

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# CHAPTER X
# MATERIALISM AND THE ORIGIN OF LIFE: II. OPARIN *versus* THE GENETICISTS

Oparin's metabolic approach to the problem of the origin of life and the genetic approach based on the concept of the primacy of the hereditary material had developed from independent backgrounds. For some time, the two approaches coexisted fairly peacefully, but during the First International Symposium on the Origin of Life, held in Moscow in 1957, the conflict between the two schools of thought became explicit. The relative priority of genes, in the form of nucleotide sequences, and of multimolecular systems of metabolism became the subject of much debate and controversy. Corollaries to this question were the debates concerning the concept of a "living molecule" (in particular nucleic acid or nucleoprotein) and discussions on the vital status of viruses.

## The Moscow debate, 1957

In the Preface to a collection of the texts submitted in advance by participants of the first international Symposium on the origin of life, Oparin listed a number of questions that remained controversial in spite of the wide acceptance of an evolutionary approach to the problem of the origin of life. Among these questions was that whether life arose in the form of individual molecules or of complex polymolecular systems. Oparin added:

> "This problem will presumably be of special interest to the participants of the Symposium as it is a matter of much debate." (1)

This prediction was fully borne out, as is clear from the transcripts of the discussions included in the complete published proceedings of the conference (2).

Norman Horowitz took up the challenge and answered Oparin's question as follows:

> "Life arose as individual molecules in a poly-molecular environment." (3)

This statement was based on the ideas that mutability, self-duplication and heterocatalysis comprise a "necessary and sufficient definition of living matter"; that the minimal chemical system exhibiting these properties is the gene; and that the chemical basis of the gene is nucleic acid. Hence, a molecule of nucleic acid could have been the first living thing on earth and, although it could not have functioned in a vacuum, its activity could have proceeded under relatively simple conditions.

Alexander Braunstein commented that one word was missing from Horowitz's "ingenious" definition: the latter part should read "in a multimolecular <u>living</u> environment", by which, however, Horowitz's central idea would be negated (4). Norman Pirie also objected to the idea of an autosynthesis of genes:

> "...it is probably the system that makes another gene, rather than the gene that makes a copy of itself." (5)

The living status of nucleic acid molecules was also maintained in the papers of two eminent virologists. Heinz Fraenkel-Conrat argued that since the nucleic acid alone of tobacco mosaic virus can perform the crucial functions of the virus, namely initiate infection and transmit the required genetic information, the origin of nucleic acid was highly relevant to the question of the origin of life (6). Similarly, Wendell Stanley emphasised the direct dependence of viruses, genes and life on nucleic acid.

He added that the crystallisation of the nucleoprotein of tobacco mosaic virus and the infective properties of this nucleoprotein had led to a "tottering" of the distinction between living and non-living matter, and that there is a continuum in size and complexity from sub-atomic particles to atoms, molecules, organisms and to the stars and galaxies (7).

Not all the virologists present adopted this attitude, however. Schramm, for example, stated in his paper that it is impermissible to regard the virus as an ancestor to life because the multiplication of viruses requires the complex enzyme apparatus of the host cell (8)*. Schramm felt that the prime interest of virus research was that it could lead to insight into the biochemical basis of multiplication and hence provide us with pertinent questions regarding the origin and evolution of mechanisms of multiplication.

A "polymolecular" view of the origin of life was adopted by most of the Soviet scientists present, including Oparin, Braunstein and A.G. Pasynskii, by pioneers in the field of the origin of life such as J.D. Bernal and Sidney Fox, and by many biochemists such as Marcel Florkin, Peter Mitchell and Erwin Chargaff. For instance, Bernal stressed the importance of the prebiotic formation of coacervates (12); while the first coacervates could not have been living organisms, it was the evolution of these systems that led to the beginning of life**.

*Similar points were made in the discussions by Pirie (9), Smorodintsev (10) and Nuzhdin (11).

**Bernal later changed his position and came out in favour of a genetic concept. In 1963 he still asked, but did not answer, the question at what stage the first coacervates appeared (13). In his book (cont. next page)

Peter Mitchell paid particular attention to the formation of systems enclosed in lipid membranes (16), which he regarded as a crucial step on the path towards the origin of life. On a more philosophical note, Erwin Chargaff asked

> "Is the cell really nothing but a system of ingenious stamping presses, stencilling its way from life to death? Is life itself only an intricate chain of templates and catalysts and products? My answer to these and many similar questions would be No; for I believe that our science has become too mechanomorphic, that we talk in metaphors in order to conceal our ignorance, and that there are categories in biochemistry for which we lack even a proper notation, let alone an idea of their outlines and dimensions." (17)

He felt that mythology had penetrated to the molecular level, beautiful legends of creation having come down to a so-called "macromolecule". He added,

> "If poetry has suffered, precision has not gained." (18)

Such a lack of precision was also implied by Oparin's summary of the discussions:

> "We may feel some regret that this gathering has not only not led to a merging of these two points of view, but has not even led to their approaching one another. However, it is clear that this required a great deal more work and would hardly have been possible at our first meeting." (19)

He made his own position clear: what had arisen by abiogenic means were not the extremely efficient nucleic acid and protein molecules encountered in present-day organisms, but polynucleotides and polypeptides of a relatively disorderly

(footnote cont.) The Origin of Life, published in 1967, he strongly criticised Oparin's concept that life had started with coacervates before an efficient mechanism of self-replication had developed (14). He suggested that life had come into being with the formation of ordered polymers of peptides and nucleotides, before separate organisms or coacervates had formed; he called this the preorganismal stage of life (15).

structure, which formed the original systems. It was only on the basis of the evolution of these individual, polymolecular systems that functionally efficient forms of molecular structures had developed, and not vice versa:

> "In the opposite case one would have to conceive of evolution as it was imagined by Empedocles, who held that first there developed arms, legs, eyes and ears and that later, owing to their combination, the organism developed." (20)

In the final discussion session, after Braunstein had again stressed the weaknesses of the concept of a living molecule, Oparin reiterated his belief that differences of opinion could not be settled by discussion, but by experimental work.

The philosophical background of this debate has been discussed by Loren Graham in his book Science and Philosophy in the Soviet Union (21) and, largely following in the latter's footsteps, by John Farley (22). In addition, Oparin has explored the philosophical issues involved in various approaches to the problem of the origin of life in his later writings. It is important, however, to keep in mind also Oparin's exhortation that differences of opinion can only be settled by experiment. The relation between the philosophical and scientific foundations of the conflict will now be examined.

Philosophical and scientific dimensions of the debate

In his perceptive chapter on the origin of life (see ref. 21), Loren Graham set out to investigate the influence of dialectical materialism on the Oparin-Haldane hypothesis of the origin of life. Both Oparin and J.B.S. Haldane had claimed an influence of this philosophy on their biological thought and both became vocal dialectical materialists.

Certainly Oparin's writings show a progressive influence of the dialectic as developed by Engels, both explicitly and implicitly. As has been shown in Chapter VII of this thesis, there is an ever-increasing emphasis on different levels of regularities in nature, within the context of a philosophy of the progressive development of matter (a "process philosophy"). It is not necessary to repeat Graham's extremely well-documented account here but a few comments are in order.

Graham suggests that Oparin's first paper on the origin of life (1924) was well within the tradition of a mechanistic approach, based on a reductionist view of life. Oparin stressed the similarities between the living and the non-living and declared that vital processes can be explained fully in terms of the general laws of physics and chemistry. Life had no special properties, but was characterised by a "definite specific combination of these properties" (23). By 1936, however, the influence of Engels' Dialectics of Nature on Oparin's thought was clear: he wrote that the laws of organic chemistry alone could not account for the transition to the higher order of the colloidal gel, nor could life be said to have come into being until a specific biological factor, namely natural selection, had come into play (24). There were two requirements for the action of natural selection: individual systems that (a) interacted with the environment (in the form of metabolism) and (b) were capable of self-reproduction, of however primitive a form. In 1924, on the other hand, Oparin had characterised the "first piece of gel" as alive in some sense. The contrast between the 1924 and 1936 works discerned by Graham is real. However, the concept of a slow progressive development of matter was already clear in the early work (and, as a concept, was not original; what was original was the detailed scientific basis given to it by Oparin, especially from 1936 onwards). In addition, Oparin had already indicated in 1924 that some transitions in the general process of development are more radical than others: the first formation of a coagulum was characterised as an extremely important stage in the development - this was when the organic material first gained structure, first became an individual* (25). Certainly, in 1924 Oparin set out a general programme for an investigation of the problem of the origin of life, consisting in a study of separate stages in the overall chain of development - the inorganic, the organic, the colloidal, and the metabolic. In this sense, his approach remained unchanged throughout his works. At the same time, he made a number of typically reductionist (mechanistic) remarks** and did not appeal explicitly to dialectical materialism. By this time, neither Engels' Dialectics of Nature nor Lenin's Philosophical Notebooks had been published, nor had the Soviet

*Farley attaches particular importance to Oparin's statement that colloidal gels would have formed by chance sooner or later (26). Oparin also stated, however, that large organic compounds were known to have a tendency to form such gels. Hence, he did not regard gel formation as a highly improbable chance event (which Farley regards as characteristic of mechanistic theories of spontaneous generation, whether of organisms or "living molecules").

**The antithesis between reductionist and dialectical materialist methodologies is not, however, clear-cut, as will be shown below.

scientific community (or the Soviet authorities, for that matter) reached a consensus on the question of the relationship of Marxist philosophy to natural science (27). Any dialectical materialist influence on Oparin at this stage would, therefore, have been fairly indirect*.

A few more remarks on the political aspects are in order. By 1930, dialectical materialism had become firmly established in all intellectual domains in the Soviet Union and Party intervention in the course of natural scientific development began. The case best known outside the Soviet Union is the Lysenko affair. (According to Graham's account, incidentally, Lysenko made use of the Marxist dialectic in a misguided, if not downright erroneous, manner (28).) In his capacity as Academician, Oparin was implicated intimately in the Lysenko affair and his political support of Lysenko is not in doubt (29). Nevertheless, as has been pointed out by Graham, Oparin did attempt to resist an invasion of Lysenkoists into his own field (30). In his own writings, he remained virtually silent on questions of genetics until the late 1950s. Regardless of any political reasons for this restraint, there were independent, scientific grounds for a cautious approach to the genetic basis of the early development of life (see below). What is clear from Oparin's writings, however, is that there was no direct correspondence between political pressures and the emphasis he placed on the dialectic. This emphasis is most pronounced in

*It is likely that Oparin was influenced by the ideas of the biochemist A.N. Bakh, with whom he was closely associated from 1921. Bakh was a revolutionary and former exile, who published on Marxism already in the 1880s.

books he published in the 1960s, at a time when ideological pressures on Soviet scientists had eased considerably.

All of Oparin's books on the origin of life start with a historical introduction and a philosophical assessment of different approaches to the question. In the book Life: Its Nature, Origin and Development, published in Russian in 1960 and in English in 1961, Oparin analysed the differences between mechanistic and dialectical concepts of life (31). His discussion centered on the dialectical emphasis on the qualitative differences between the living and the non-living. Once life had come into being, on this view, the laws of physics and chemistry continue to operate but are supplemented with new biological laws that do not operate in the domain of matter in general, but only in living matter. In contrast, the mechanist sought to explain life exhaustively in terms of physics and chemistry alone and, in effect, denied the special features of life. Among the special features of life was the constant renewal of the constituents of living systems by material exchange between the organism and its environment. This material exchange as such was common to all open systems, but characteristic to the metabolism of living systems was the strict coordination of metabolic reactions in space and time. Moreover,

> "...The whole of this sequence is directed in an orderly way towards the continual self-preservation and self-reproduction of the living body as a whole." (32)

According to Oparin, this "purposiveness", as expressed by the organism's adaptation to the environment, was also an essential feature of life and any consistent account of the origin of life had to explain the origin of this feature. The explanation should be given, not in terms of some idealistic principle such as Aristotle's entelechy, but in terms of the Darwinian principle of natural selection. Hence, at this time, well-coordinated metabolism, self-reproduction and "purposive" adaptation were the fundamental characteristics of life to Oparin.

In a later work Oparin explained clearly why the formulation of the qualitative differences between life and non-life was important (33): while a detailed analysis of the substances and processes of living organisms in chemical terms is extremely important, as witnessed by the brilliant success of biochemistry, such investigations are not sufficient for a full understanding of the nature of life. In Oparin's opinion, it is only by establishing the precise qualitative distinctions of life that we can gain insight into its nature. The reductionist, who in essence denies the genuine development of life, has no means of asking the appropriate questions relevant to the problem of its nature and origin. This, of course, is a methodological argument and Oparin's objections to the concept of a "living molecule" were also given in methodological terms: any theory that depends on a "lucky chance" is methodologically unsatisfactory because it does not tell us what kind of questions to ask or what kind of investigations to carry out. The argument, reiterated in his later works, was already given in a nutshell in the third (completely revised) edition of his 1936 account, published in 1957. In the context of a discussion of Muller's views, Oparin wrote:

> "A theory is of special value to the scientist if it opens up practical possibilities for research by verifying the regular occurrence of phenomena, either by observing nature or by setting up suitable experiments in the laboratory. The concept of the chance development of living molecules is quite unproductive practically." (34)

This really is the crux of the matter and accounts for the success of Oparin's theory, who could take into account a mass of relevant scientific data, and for the comparative fruitlessness of the genetic approach in so far as it relies on the fortuitous formation of a living molecule. Of course, in metaphysical terms, there is nothing inherently impossible about the idea of the occurrence of a single chance event, however improbable. It is not, however, conducive to empirical scientific progress.

In addition, both Graham and Farley have rightly commented on the reductionist basis of the arguments used by the adherents of the genetic approach at the Moscow Symposium (35). It is important to realise, however, that the methodological objections apply to a particularly extreme form of reductionism only, namely that which aims to reduce all vital processes to the properties of single molecules (the nucleic acids in this case). Few biochemists are reductionists in this sense. The aim of biochemistry is to explain vital processes in terms of the properties of sets of molecules <u>and their interactions</u> under specific initial conditions. No fundamental laws of physics and chemistry are violated under these specific initial conditions (describable in terms of the organism and its immediate environment) but the fundamental, universal laws <u>per se</u> are no longer necessarily of primary interest. Of course biochemists study single molecules and single systems, such as enzymes or cell membranes, respectively. The ultimate aim of such investigations, however, is to elucidatethe functional relationships within and between individual systems, for example systems of metabolism or energy transfer. It is not clear that there is a fundamental conflict between dialectical materialism and the biochemical-type of reductionist approach, especially if the latter is based on the notion of correspondance principles leading from one level of complexity to another*.

What is important is that the historical dimensions of life are acknowledged and understood. There is a difference between E. coli and the elephant and it must be assumed that there was a difference betweenthe first living systems on earth and E. coli. While an evolutionary approach to biological questions is not the prerogative of dialectical materialism (Charles Darwin managed without the dialectic, as have many evolutionists), the dialectical emphasis on historical processes provides an important heuristic stimulus in this respect.

Throughout the history of Marxist philosophy, it has been

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*There certainly is no conflict between this approach and the following statement made by the Marxist philosopher S.T. Melukhin:

> "Natural material systems are complete and integrated only if they fulfil the following two conditions: (1) there is interaction between their elements by means of exchange of matter and motion (and also information in self-organising, self-controlled systems); (2) *there is a unified quantitative law (or set of laws) of interaction of the elements and causal connection between the previous and subsequent states of the system*, that is, unified laws of genetic determination. If these two conditions or criteria are not fulfilled, there can be no integral system; what we have is merely a conglomeration of elements, accidentally connected with one another." (36) (italics added - HK).

emphasised that concrete problems in natural science cannot be solved by the dialectic alone, but only by "an alliance of dialectics and concrete scientific research" (37). The role of the dialectic is above all a heuristic one:

> "...The theoretico-cognitive aspect of dialectical materialism ...... does not, as a method, as a guiding principle of investigation, provide absolute solutions to problems, but primarily assists in their proper framing." (38)

The empirical content and general scientific background of the metabolic and genetic theories of the origin of life are therefore highly relevant in a discussion of the conflict between these two positions*. It is in this respect also that the difference between the two schools of thought was particularly clear. While successive editions of Oparin's work reveal a progressive theoretical development, based on scientific, and especially biochemical, advances, the factual basis of the "living molecule" concept was somewhat thin and the concept itself remained static for many years. The determination of the structure of the hereditary material led to an identification of the living molecule with DNA, or at least a functional DNA precursor. The basis of DNA function in gene transmission and gene expression (or what used to be called its "auto- and heterocatalytic properties") remained to be elucidated. Before the role of the nucleic acids in protein synthesis even began

*This is clearly realised by Graham, who wrote that a full history of Oparin's theories must take into account the biochemical background, not only dialectical materialism (39).

to be clarified*, DNA was not uncommonly used as a kind of "God of the gaps", that is, it was invoked to conceal ignorance. This aspect is also discernable in the living molecule approach to the origin of life and has been commented on by several authors. Oparin himself has characterised the approach as "metaphysical" on those grounds. Similarly, Keiosian has written,

> "The gene theory is thus also an origin of life theory by edict. There is also an element of mysticism in it. The gene has been made the repository of all of the mystical powers of the 'élan vital' of the vitalists." (41)

The same sentiment was expressed more forcefully by Chargaff, when he wrote of the double helix having been elevated into "the mighty symbol that has replaced the cross as the signature of the biological analphabet" (42).

At the time of the Moscow Symposium, it had become clear that there must be a relationship between DNA and protein synthesis even if the nature of this relationship was not understood. Indeed, two out of the seven sessions of the Symposium were concerned with the origin of proteins, nucleoproteins and enzymes, and several of the papers dealt with the complex relations between the nucleic acids and the proteins. A mutual dependence between the two types of substances in contemporary organisms was evident and gave rise to the question, which is

*The mechanisms of control of protein synthesis are still not fully understood, especially with respect to the eukaryotic cell. This also means, incidentally, that classical Mendelian genetics is not yet reducible to molecular genetics, as has been claimed by some philosophers of biology (40). Such a reduction would require a much better understanding of the molecular basis of the control of gene expression and the genotype-phenotype relation than is available today.

still being asked occasionally, which came first, DNA or protein. In fact, the question had been raised by J.D. Bernal in a lecture he delivered in Moscow in 1955. In the third edition of his classic book, Oparin answered as follows:

> "This question reminds one somewhat of the scholastic problem about the hen and the egg. The problem is insoluble if we approach it metaphysically in isolation from the whole previous history of the development of living matter. Nowadays every hen comes from an egg and every hen's egg from a hen. Similarly, nowadays proteins can only arise on the basis of a system containing nucleic acids while nucleic acids are formed only on the basis of a protein-containing system. The hen and its egg developed from less highly organised living things in the course of their evolution. In the same way, both proteins and nucleic acid appeared as the result of the evolution of whole protoplasmic systems, that is to say, from whole systems and not from isolated molecules. It would be quite wrong to imagine the isolated primary origin either of the proteins or the nucleic acids". (43)

The complexity of the nucleic acid-protein relation subsequently received a solid empirical basis. In 1960, Arthur Kornberg demonstrated that DNA replication could take place in the test tube, using a "DNA synthesising enzyme" (DNA polymerase) isolated from Escherichia coli (44). The vast apparatus of enzymes that is known to be required for DNA-directed protein synthesis has complicated the picture: in contemporary organisms at least the nucleic acids are not enough to produce protein synthesis. Certainly, current adherents of the "living molecule school" no longer think in terms of explaining the origin in the prebiotic soup of the highly specific and complex proteins and nucleic acids encountered in contemporary organisms, but in terms of very much simpler oligonucleotide and oligopeptide chains. They do, however, continue to think in terms of a molecular evolution taking place in the general environment of the primaeval earth, rather than in confined open systems. Despite the spectacular advances of molecular biology in the last few decades, however, this approach has not yet led to a hypothesis based solidly on chemical theory or on empirical evidence*. Ironically, it was Oparin who made potentially fruitful use of molecular biological developments, within the context of his concept of a multimolecular origin of life. A brief summary of his remarks on molecular genetics will be given below with a view to showing that a synthesis between the metabolic and the genetic approaches, but in a multimolecular framework, is now within the realms of possibility.

Towards a synthesis?

Muller's statement on Oparin's anti-genetic outlook, quoted in the previous chapter (page 301), was made in 1966. It is true that Oparin paid no attention to the origin of a specific genetic material or system in the first edition of his book. It should be pointed out, however, that the evolution of a material genetic apparatus within preformed coacervates was in no way excluded. It is also relevant that in 1936, when Oparin's book appeared in print, there was much uncertainty about the chemical nature of genes and their functions - it was not clear whether genes were composed of proteins, nucleic acids or nucleoproteins. In other words, even if Oparin had wanted to say anything about the evolution of genetic systems, he could not easily have done so in concrete terms.

*The same point was made by Florkin; in 1975, he wrote that the gene hypothesis of the origin of life still had no experimental basis (45).

An examination of Oparin's later works, however, exposes Muller's accusation as totally unjustified. In the 1957 edition of his book, Oparin included a chapter entitled Tho Structure and Biological Functions of Proteins and Nucleic Acids and the Problem of their Origin (46), including no less than 210 references. A major part of this chapter is devoted to a discussion of the role of nucleic acids in replication and protein synthesis. Here Oparin carefully reviewed the evidence showing that DNA is the genetic material, the evidence for the role of DNA and RNA in protein synthesis, recent research on viruses, and research on the structure of the nucleic acids, including a discussion of Watson and Crick's double helical model. He fully recognised the importance of the latter and explained how it had given rise to the concept of a genetic code. He presented an account of Gamow's proposal of a code based on nucleotide triads*, describing the latter as "very ingenious". He also pointed out that much more experimental work was required before such suggestions could be accepted, however - a remark fully borne out by later

*Gamow, who proposed various possible codes, based his nucleotide triad hypothesis on mathematical considerations: The four different nucleotides of any particular nucleic acid were to be taken in groups of three. Each triad could then either be composed of three identical units, or of two identical components and one different unit, or all three components could be different. The number of variants would be 20, which corresponds to the number of amino acids that make up proteins in living organisms. (Note that the number of possible variants is 20 only if the order of nucleotides in each triad is irrelevant. The triplet code accepted now does distinguish between, say, AAC, ACA and CAA, and there are 64 variants. This code is highly redundant, some triplets functioning as stop or start signals and some different triplets coding for the same amino acid.)

developments. The crucial question remained:

> "How is the rigidly determinate arrangement of nucleotides in the polynucleic matrix set up?" (47)

What a theory of the early development of life had to explain, wrote Oparin, was how the specificity of the nucleotide sequences in nucleic acids and of the amino acid sequences of proteins had come into being. The origin of this specificity of structure could not be explained simply on the basis of universal laws of thermodynamics and chemical kinetics, but had to be seen as the result of a long process of evolution, of "purposeful" adaptation within increasingly better and more highly organised systems. In other words, the evolution of nucleic acid and protein structures had gone hand in hand with the evolution of metabolism.

A similar account was included in Life: Its Nature, Origin and Development, published in 1960. Here Oparin particularly emphasised the role of RNA in protein synthesis and its link with metabolism by way of enzymes. He suggested that the RNA-protein relationship had come into being before DNA played any part in pre-cellular systems (48), a suggestion that had been made previously by Belozerskii at the Moscow Symposium (49). Oparin wrote that this possibility could only be explored further once the genetic code had been definitely established. Two years later Alexander Rich presented a more elaborate treatment of the idea that an RNA-like polymer which could convey genetic information as well as organise amino acids into specific sequences was the hypothetical stem molecule of present-day DNA and RNA species (50). Rich wrote in terms of evolution at the molecular level in the general environment. Oparin adapted the idea to a polymolecular concept of the origin of life in his book Genesis and Evolutionary Development of Life, published in Russian in 1966 and in English in 1968 (51).

Briefly, Oparin's argument ran as follows: A random polymerisation of peptides and nucleotides could have taken place in the general environment of the prebiotic earth. The presence of high-molecular-weight polymers (including polypeptides and polynucleotides) would have led to the formation of coacervates. Those coacervates which exhibited dynamic stability and were capable of interacting dynamically with the environment as well as growth formed the main line in the development of life; they may be termed "protobionts". Initially, the protein-like polymers present in protobionts were random and non-ordered and had little or no catalytic activity. For the further evolution of protobionts, it was important that some sort of organisation developed within the systems, which permitted the synthesis of polypeptides with a more or less stable amino acid sequence. Those protobionts in which functionally effective polypeptides developed gradually would be favoured by natural selection. The nucleic acids (or their precursors) would have played a crucial role in the development of the intramolecular stability of polypeptides. DNA, however, lacks a hydroxyl group at the second carbon of the deoxyribose moiety and cannot bind amino acids directly, as can RNA. In this respect the role of tRNA, which lines up amino acids in sequence in protein synthesis, is particularly relevant. And because the RNA viruses provide proof that RNA can also act as a carrier of information, it is likely that the hereditary role of the metabolically comparatively inert DNA represents a later specialisation. Clearly, there is much missing from this account and several questions remain to be answered:

(1) How did the ordered polymerisation of RNA-like molecules necessary for an ordered lining up of amino acids, arise?

(2) How exactly did the RNA-protein relationship arise?*

(3) How did the specialisation of RNA-like molecules into mRNA and tRNA species arise and at what stage did ribosomal RNA enter the picture?

(4) How did the DNA-RNA relationship and the genetic code arise?

However, once again Oparin presented a programme of potentially great heuristic importance. Oparin and his co-workers have been investigating RNA-containing coacervate models and although many questions remain, an experimental approach may lead to further major developments. The above account also illustrates how effectively Oparin has been able to incorporate new scientific developments in his theory. His theory remains a developing one, always open to further elaboration. The

*More recently, Crick and coworkers have presented some interesting speculations on this point (52). Their paper suggests how protein synthesis may have been possible with only mRNA and a few different tRNA molecules (the latter are assumed to be similar to present-day ones). However, besides being speculative and without experimental basis, as the authors admit, the primary motive underlying the proposal appears to have been the attempt to demonstrate that ribosomes may not always have been essential for protein synthesis. While Oparin and his followers would presumably agree that the ribosomes are comparatively advanced products of evolution, they would probably object to the implication that a mechanism for the ordered synthesis of protein could have evolved freely in the general prebiotic environment.

empirical basis of the theory is absolutely essential, and that is as it should be in a dialectical context.

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## Chapter XI

## THE PRESENT STATUS OF THE PROBLEM OF THE ORIGIN OF LIFE

Investigations into the origin of life have expanded rapidly over the last 25-30 years and the scientific literature on the subject has grown accordingly. Many reviews of the experimental and theoretical advances made in the field are available* and it is not the intention here to add to their number. The aim, rather, will be to discuss briefly the principles underlying current investigations of the problem of the origin of life and to outline some areas where fundamental problems remain to be solved.

### The experimental phase

The foundations for an experimental approach to at least some of the hypothetical stages in the development of life from non-living matter were laid by Oparin's theory. Three areas in particular have been investigated extensively: the abiogenic synthesis of organic compounds under putative prebiotic conditions; the behaviour of models of precellular systems such as coacervates; and comparative studies of the mechanisms of energy metabolism in a wide range of species.

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*Besides Oparin's books (see Bibliography), several useful monographs by other authors have appeared. Among those recommended are The Origin of Life by Natural Causes by Martin Rutten (1) and Chemical Evolution by Melvin Calvin (2). A comprehensive review of the field is included in the second edition of Lehninger's textbook of biochemistry (3) and several valuable reviews of particular areas in the field are presented in Part I of Exobiology, edited by Ponnamperuna (4). The quarterly journal Origins of Life (formerly Space Life Sciences) is devoted to studies of the origin of life, as is a large proportion of the papers published in the journal Biosystems.

Abiogenic organic synthesis: In 1953 Stanley Miller reported the formation of significant amounts of amino acids from a gaseous mixture of methane, ammonia, hydrogen and water circulating past an electric discharge (5). Paper chromatography revealed the presence in the aqueous phase of glycine, alanine and other common amino acids. Miller's experiments were performed in an attempt to test Oparin's hypothesis that organic compounds are formed readily from simple starting compounds in a reducing atmosphere. The results supported this hypothesis and stimulated a great number of experiments in the new field of "prebiotic chemistry". By the early 1970s an impressive array of organic molecules that play a role in living organisms had been synthesised abiogenically under a variety of possible primitive earth conditions. These molecules include at least 15 of the 20 common amino acids, the purines adenine and guanine, the pyrimidines cytosine and uracil, sugars (including ribose and deoxyribose), nucleotides (including ATP), fatty acids, porphyrins, polypeptides, polyphosphates and oligonucleotides (6).

The conditions under which these molecules have been synthesised are not uniform. However, conditions on the earth were (and are) not uniform and there are several environments to choose from: the atmosphere, the oceans, the lithosphere and many micro-environments such as hot springs and brackish tidal pools. It is important, however, that the conditions for the formation of different compounds that were required for further chemical evolution are at least mutually compatible*. In this respect,

*A second requirement, of course, is that the molecules are not broken down readily under the conditions in which they are formed.

it is encouraging that the conditions for the abiogenic synthesis of amino acids (the case that has been investigated most extensively so far) have turned out to be very flexible. Reviewing this area in 1959, Miller and Urey could show that amino acid synthesis is activated by a wide range of sources of energy, for example electric discharges, ultraviolet light, cosmic radiation, thermal energy and radioactive $\beta$-decay. Moreover, amino acids are formed from many different combinations and proportions of the gases $H_2$, $CH_4$, $CO$, $CO_2$, $NH_3$, $N_2$, $H_2O$ and $O_2$, with the proviso that the reactions proceed readily only if the overall conditions are reducing (7). An analysis of the possible reaction mechanisms and the intermediates that had been isolated also indicated that a rigid set of conditions is not required: any process, or combination of processes, that yields HCN and aldehydes would have contributed to the formation of amino acids in the primitive oceans*.

This flexibility of conditions, which has since been confirmed in numerous other experiments and for products other than amino acids, is of great importance in view of the fact that earlier ideas of a strongly reducing primitive atmosphere have recently been challenged (9). Astrophysical models** and geochemical

*The most plausible reaction scheme is the following: first HCN and aldehydes are synthesised in the gas phase, activated by an energy source. The aldehydes and HCN react in the aqueous phase to give amino- and hydroxynitriles which are then hydrolysed to amino and hydroxy acids (8).

**In terms of distance from the sun, size and rocky composition, the earth most closely resembles Mars and Venus, both of which have large amounts of carbon dioxide in the atmosphere. Models taking into account the different surface temperatures of the three planets and rates of degassing suggest that the earth's atmosphere also has always contained carbon mostly in the form of $CO_2$ (10).

evidence* now suggest that the earth's early atmosphere may have been only mildly reducing, consisting of carbon dioxide, water vapour, free nitrogen and probably some hydrogen. The absence of significant amounts of free oxygen is generally agreed upon, which is of importance in relation to the stability of newly formed organic matter. Hence, although Oparin's and Miller and Urey's ideas of a primitive atmosphere rich in methane and ammonia may have to be abandoned, and although some abiogenic syntheses may have to be repeated under more plausible conditions**, the general idea of prebiotic chemical evolution has not come into question. The primary requirement that hypotheses of chemical evolution should be consistent with astrophysical and geochemical theory is still fulfilled despite recent shifts in emphasis from

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*The presence of $CO_2$ in the early atmosphere is indicated by the carbonate mineral content of rocks in Greenland that are $3.8 \times 10^9$ years old (11). Geochemical evidence does, however, suggest that conditions on earth in Precambrian times were at least mildly reducing. For example, the sands and gravels associated with the gold-uranium reefs in the South African Witwatersrand basin show striking differences in composition according to their age: the newer sands are composed almost exclusively of quartz ($SiO_2$) whereas the older sands contain large amounts of other minerals, such as pyrite ($FeS_2$) and uraninites, that are not stable under an oxidising atmosphere (12).

**This may not in fact be essential in view of evidence that even now local, as opposed to global, levels of highly reduced gases are high. For example, the photochemical reduction of atmospheric nitrogen to ammonia is catalysed by titanium dioxide and certain desert areas rich in titanium are estimated to generate as much as 1-10 kg of ammonia per acre in a year by such photochemical reduction (13). (In fact, titanium dioxide is also an effective catalyst in the abiogenic synthesis of amino acids; in the presence of this catalyst, the reactions proceed with energy sources no stronger than ordinary sunlight.) Highly reducing conditions are also encountered in the sterile environment of Red Sea brine, which is rich in methane, ethane and low-molecular-weight paraffins. Since the discovery that thiocyanate is present in Red Sea brine, it has been suggested that abiogenic synthesis of amino acids may take place in this environment even at the present time (14).

a strongly to a weakly reducing atmosphere.
Models of precellular systems: According to Oparin's theory, the next stage after the formation, accumulation and transformation of organic matter on the primitive earth was the formation of coacervates, which evolved into the first metabolising systems. The spontaneous formation of coacervates in dilute solutions containing as little as 0.001% of organic polymers suggested an attractive model for precellular systems and such models have been investigated extensively by Oparin and his co-workers (15). Coacervates of many different compositions show selective absorption of materials (such as dyes and amino acids) from the medium, growth by concentration of absorbed material, differentiation in composition due to internal chemical changes, phenomena resembling pinocytosis (such as the ingestion of microscopic oil droplets) and the formation of colonies (which might lead to greater complexity by exchange of material or by fusion) (16). Oparin's group has succeeded in making "dynamically stable" coacervate drops which interact with the medium in the manner of open systems, thus allowing for further development of the system. By the use of appropriate materials*, it has been possible to simulate such processes as enzymic synthesis (including polynucleotide synthesis) and enzymic decomposition, oxidation-reduction reactions, photochemical processes and even phosphorylation reactions coupled with oxidoreduction (17). For example, the addition of glucosyltransferase and glucose-1-phosphate to the

*Most of these materials were obtained from biological sources. This aspect of the experiments will be discussed below.

medium of gum arabic-histone coacervates resulted in the synthesis of starch inside the coacervates; the addition of β-amylase led to the breakdown of starch and the release of maltose into the medium. The addition of chlorophyll-containing coacervates to a medium containing ascorbic acid and methylene red resulted, upon illumination with visible light, in the light-activated oxidation of ascorbic acid and reduction of the dye. Invariably, these reactions proceeded much more rapidly within the coacervates than in the medium, because the materials are concentrated inside the droplets.

Closely related to the coacervate studies are experiments that have been performed with lipids and proteins in aqueous solution (18). The protein-lipid complex model is of particular interest because lipoprotein vesicles with structures that closely resemble biological membranes are formed readily by the agitation (for example by the action of wind) of protein-lipid films at air-water interfaces (19).

A different model, that of proteinoid microspheres, has been studied extensively by Sidney Fox and his colleagues (20). This work arose out of studies of the thermal copolymerisation of amino acids. Because peptide-bond formation involves dehydration and proceeds more readily in the absence of water, Fox postulated that the prebiotic formation of protein-like polymers must have taken place at very high temperatures, for example in a volcanic environment. Most amino acids decompose on heating, but Fox found that dry mixtures of amino acids enriched with dicarboxylic amino acids (glutamic and aspartic acid) form large linear polymers after exposure to temperatures up to 170°C. In the presence of phosphates the amino acids copolymerise even at 65°C (21). Fox called those polymers "proteinoids" because of their striking resemblances to biological proteins: the proteinoids are of high molecular weight (up to 300,000), they show spontaneous ordering due to selective interactions of amino acid molecules of different shapes, they exhibit weak catalytic activity (including hydrolysis, decarboxylation, deamination and oxidoreduction), they bind polynucleotides and they have nutritive value for some bacteria. When hot mixtures of proteinoids come into contact with water or aqueous salt solutions, they form "microspheres" and these microscopic proteinoid units share some properties with contemporary cells: the microspheres react to osmotic pressure by swelling or shrinking, they absorb material from the medium, have weak catalytic activity, are surrounded by multiple boundary layers and they "reproduce" by budding after accretion of new proteinoid material. In view of these properties, Fox has called the proteinoid microspheres "protocells" and postulated that, with the development of mechanisms of energy metabolism and of molecular mechanisms of replication, these protocells evolved into bodies resembling contemporary cells (22).

Both the coacervate model and the proteinoid model have been tested for their "evolutionary relevance" by Rohlfing (23). The criterion of evolutionary relevance, which any prebiotic model must fulfill, has two components: that of evolutionary continuity, which demands that there must be an explanation for the source of the constituents of the system; and that of environmental relevance, which demands that the formation and behaviour of the system are modelled on realistic prebiotic environmental conditions. In the experiments of Oparin and his group coacervates were made using polymers of biological origin and the source of these materials in a prebiotic context has not been explained. Hence, the models fail to meet Rohlfing's criterion of evolutionary continuity. However, the significance of this failure depends on the function of the model: were the particular coacervates used in the experiments intended to represent realistic prebiotic systems or were they designed to investigate the detailed behaviour and potential for development of coacervates in general*? In the experiments of the Moscow group, the latter aim has been primary and no claims for realism have been made. Nevertheless, it would be highly desirable for future work in this field to simulate prebiotic conditions more closely. For example, enzymes from biological sources should only be used (for convenience) if it has been shown experimentally that the same reactions take place (albeit less efficiently) with the use of simple catalysts that are likely to have been available in the prebiotic environment.

The proteinoid model does meet the criterion of evolutionary continuity because proteinoids are formed from materials

*The evolutionary relevance of the coacervate model in general is not questioned - what is questioned is the validity of using materials that presumably are the products of biological evolution.

produced under simulated prebiotic conditions*. Rohlfing, however, has questioned the environmental relevance of certain aspects of Fox's model for the formation of proteinoids. For example, proteinoids are synthesised artificially from amino acid mixtures rich in glutamic and aspartic acid. However, this preponderance (which, incidentally, is also encountered in contemporary biological proteins) is never produced in simulated prebiotic syntheses of amino acids, where glycine and alanine are the most abundant products. Moreover, such syntheses also yield amino acids that are not among the common constituents of contemporary protein, while Fox has always used mixtures of proteinous amino acids. Using the types and proportions of amino acids produced under simulated prebiotic conditions, Rohlfing found that these sets of amino acids do undergo thermal copolymerisation but that the composition of the resulting proteinoids differs from those studied by Fox's group. The predominant constituent of Rohlfing's proteinoids was glycine and not the dicarboxylic amino acids (even in one case where glycine was not the most abundant of the reactant amino acids), and the polymers contained non-protein amino acids. Rohlfing also tested the effects on proteinoid formation of using different atmospheric pressures, atmospheres composed of different sets of

*Fox also favours the thermal formation of amino acids themselves, a process which requires extremely high temperatures (about 1000°C). Fox's entire thermal scheme requires high temperatures alternating with periods in which liquid water is present (24). Although Fox has argued that volcanic regions with periodic rainfall were prevalent on the prebiotic earth, many have questioned the plausibility of the required conditions (25). However, proteinoid formation as such is not strongly dependent on these conditions, nor is microsphere formation.

gases* and the use of samples of amino acids contaminated with various geological materials. In all cases proteinoids were formed and the only modification of the proteinoid model suggested by the experiments concerned their composition. In other words, criteria of environmental relevance confirm the general validity of the proteinoid model but suggest specific refinements.

Discussing proteinoid microspheres, Rohlfing noted that particles made from lysine-rich proteinoids show a number of marked resemblances to coacervates and suggested that further work be directed at the merging of the two models with a view to devising an artificial protocell which fully meets the criterion of evolutionary relevance. Once this goal is achieved, it may be possible to investigate systematically how complex, co-ordinated systems of metabolism and molecular mechanisms of reproduction might have evolved. These areas are still very obscure, which means that ideas on the actual transition to living organisms resembling contemporary organisms in their fundamental characteristics as yet have no experimental basis.

Comparative biochemistry: The third class of investigations that are relevant to Oparin's theory of the origin of life is represented by comparative biochemical studies, which may provide some clue to the early evolutionary development of life. Any information gained from such studies is, by necessity, indirect and great care must be taken in the extrapolation of data obtained from contemporary organisms to their primitive

*It is of particular interest that the composition of the atmosphere did not affect the yield, the composition or the tested properties of the polymers.

ancestors. Contemporary organisms that are designated primitive are in fact the products of billions of years of evolution and show a combination of archaic and specialised features.

The general concepts of molecular and biochemical evolution have been discussed by Florkin (26). The approach of molecular evolution is based on the idea that evolutionary relationships between organisms are reflected in relationships between DNA sequences and, via the genetic code, in the amino acid sequences of proteins. Proteins from different species that show chemical kinship are called isologous; those that show functional similarity analogous. Proteins that have a degree of isology higher than that expected on the basis of chance mutation may be used as a measure of homology, i.e. genetic kinship. Analogous proteins, on the other hand, need not be homologous. For example, the aldolases involved in glycolysis in yeast and in mammalian muscle, respectively, are analogous but show insufficient chemical kinship to warrant an assumption of common ancestry (27). Nor are all homologous proteins analogous; for example, the haemoglobins and myoglobins of vertebrates are homologous but perform very different functions. When molecules other than nucleic acids and proteins are considered, isologous molecules are only assumed to indicate homology if the pathways of their synthesis is the same, in which case the homology ultimately applies to the enzymes that coordinate the biosynthetic pathways.

Using these concepts, it has been possible to construct phylogenetic trees on the basis of the degree of isology of proteins that have retained the same function through evolution. The concept of molecular evolution has received much support from the agreement between these phylogenetic trees and those obtained on independent, comparative anatomical, physiological and palaeontological grounds.

In the case of bacteria, however, matters are less clear-cut. Fewer comparative molecular data are as yet available than for higher organisms, the taxonomy of contemporary bacteria remains a problematic and controversial subject, and independent checks (such as a reasonably representative fossil record) are lacking. Those data that are available tend to confirm the general sequence proposed by Oparin in 1936; anaerobic heterotrophs preceded photoautotrophs and the latter preceded aerobic heterotrophs (see Chapter VII). The second step is supported by sequencing studies of the c cytochromes* (28), for example, and both steps are supported by studies of the ubiquitous ferredoxins (iron-sulphur proteins) (29). However, the most interesting information on the early development of life has, so far, been provided by comparative biochemical rather than comparative molecular studies. Comparative biochemistry involves the study of the biochemical mechanisms whereby different species perform certain vital functions. Overall mechanisms may of course be analogous without having a common origin, but the isolation of enzymes and intermediates in the reaction chains may provide stronger indications of homology.

*The first transition cannot be studied in this case because cytochrome c is absent in the anaerobic fermenters.

In 1936, and subsequently, Oparin based his sequence of the evolution of primaeval organisms on studies of the mechanisms of energy transformations in contemporary organisms, a field that has since expanded greatly and become much refined. The elucidation of molecular mechanisms of energy transformation in a vast number of organisms has confirmed the general sequence proposed by Oparin in 1936. The main observations can be summarised in general terms as follows (30). Coupled oxidation-reduction reactions (electron transfer) integrated with phosphorylation reactions and the production of high-energy intermediates (such as ATP) form the basis of metabolism in all living organisms. The glycolytic pathway, involving the phosphorylation of organic substrates and the net production of ATP from phosphorylated intermediates, is the primary mechanism of energy transformation in anaerobic heterotrophs and has been retained throughout evolution. In photosynthetic organisms, mechanisms of coupled phosphorylation and electron transport are more complex and more efficient: a cyclic component has been added to the electron-transfer system, opening up possibilities of regulation by feedback mechanisms. (In higher plants the electron-transfer system has a more varied set of electron carriers than that in photosynthetic bacteria and additional electron-transfer cycles may arise.) In respiring aerobes the electron-transport chain is fundamentally the same as that of photosynthetic organisms, but the utilisation of oxygen is accompanied by the addition of the respiratory chain and novel sets of enzymes (31). This superposition of


Prokaryotic evolution based on bioenergetic mechanisms.
Examples of modern representatives are given in the top row.

novel mechanisms on existing ones suggests an evolutionary sequence.

Bioenergetic studies also suggest intermediate stages in this general sequence. To give a few examples, in anaerobic conditions, the photoorganotrophs (such as the non-sulphur purple bacteria) combine fermentation reactions with partially developed photosynthetic mechanisms. Some mutants of the photosynthetic blue-green alga Scenedesmus revert to photoorganotrophy. There are great variations in the efficiency of oxidative metabolism, as measured by P/O ratios, among extant bacteria; it is particularly low among the chemosynthetic bacteria which use inorganic substrates as electron donors and these may be modern equivalents of some of the earliest aerobic organisms.

Current knowledge suggests the following sequence for prokaryotic evolution (see diagram*): (a) anaerobic, obligate fermenters resembling extant clostridia; (b) anaerobic photoorganotrophs, which made best use of the limited amount of fermentable substrates in the environment by the additional use of light-driven reactions; (c) anaerobic photolithotrophs, or photosynthetic bacteria, which utilised inorganic substrates such as sulphides as electron donors (some modern photolithotrophs are partially aerobic); (d) anaerobic phytophototrophs such as the photosynthetic blue-green algae, which used water as electron donor (all modern equivalents are aerobic); (e) chemolithotrophs (chemosynthetic bacteria) which used inorganic

*The diagram is based on the evolutionary sequence presented by Broda (32). The same sequence is implicit in the review by B.A. Rubin, quoted in refs 30 and 31.

electron donors and utilised oxygen released by the phytophototrophs; these probably descended from the photolithotrophs; (f) non-photosynthetic facultative aerobic respirers (resembling, for example, E. coli), descended from anaerobic photoorganotrophs; (g) and, evolved from the latter, strictly aerobic, non-photosynthetic respirers.

The main difference between this scheme and that proposed earlier by Oparin concerns the evolutionary relationship between photosynthesis and oxidative respiration. Oparin suggested that, with the availability of oxygen in the air, anaerobic heterotrophs developed mechanisms of oxidative respiration, bypassing the photoautotrophic branch altogether. The similarities of the electron-transport systems of aerobic respirers and photoautotrophs, however, suggests a close evolutionary relationship. It is now thought more likely that the only strictly heterotrophic branch to diverge directly from the anaerobic fermenters is represented by oxygen-tolerant ("microaerophilic") fermenters such as the lactic acid bacteria (33).

It should be pointed out that the sequence detailed above is based on a monophyletic origin of the prokaryotes. This idea has been challenged on the basis of RNA sequencing studies (34), but the alternative hypothesis of three main lines of phylogenetic development is as yet highly controversial and, in fact, does not affect the "bioenergetic sequence" within the main prokaryotic branch. Many more data will be required before an investigation of the possibility of parallel evolution of mechanisms of energy transfer is warranted.

In conclusion, all three classes of experimental investigation outlined above have lent support to Oparin's theory in its general outlines although modifications in detail have proved necessary. The major questions remain in the area of the transitions that took place between the accumulation of organic matter on earth and the appearance of the ancestral obligate fermenters. Here much experimental work remains to be done and a fruitful interaction between theory and experiment can only lead to stronger hypotheses.

Who is the Potter, pray, and who the Pot?

"Chicken-and-egg" questions have plagued students of the nature and origin of life for centuries. A number of variations on this general theme continue to pose philosophical and methodological problems. For example, is it necessary to formulate hypotheses on the development of organic catalysts with a high degree of specificity in the prebiotic environment prior to the origin of primitive organisms, as Calvin has attempted to do (35)? Or can it be assumed, as Oparin and others have done, that the specificity of modern enzymes is the result of prolonged biological evolution? Secondly, as has been indicated in the previous two chapters, one school of thought believes that the primary aim in the field of the origin of life should be to explain how the nucleic acid/protein relationship based on the genetic code arose. The opposing school of thought believes that the genetic code is the product of biological evolution. But perhaps the most fundamental formulation of the chicken-and-egg question concerns the origin of the molecular asymmetry of living organisms (36).

Molecular asymmetry and life: Most of the organic constituents of living organisms are asymmetric*. Ordinary laboratory synthesis of asymmetric molecules from symmetric starting compounds invariably results in a racemic product, because the probabilities of forming either enantiomer are equal and sufficiently large numbers of molecules are involved for the law of averages to apply. In living organisms, however, asymmetric molecules are always found in one form and when an organism synthesises an asymmetric molecule it invariably makes the same enantiomer each time. With very few exceptions, the chirality of each type of molecule is uniform throughout the living world. For example, all naturally occurring sugars and nucleotides are of the D-configuration and the amino acids that make up proteins are exclusively of the L-configuration**. The ability to synthesise and accumulate one enantiomer of each asymmetric molecule selectively is a characteristic feature of all known organisms, but appears to be absent from inanimate nature. This fundamental difference between the living and the non-living world has been a

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*Assymetric, or chiral, organic molecules are those that contain an asymmetric carbon atom, that is, a carbon atom to which four different groups or atoms are attached. Depending on the relative arrangement of these groups or atoms, such molecules can adopt two steric configurations (traditionally called the D- and L-configurations), one being the mirror image of the other. The two steric forms of the molecule, or enantiomers, have identical chemical properties but can be distinguished by physical means: each enantiomer is optically active in the sense that it will impart either a clockwise rotation (dextrorotation) or an anticlockwise rotation (laevorotation) to the plane of plane-polarised light traversing them. A mixture of equal numbers of the two enantiomers is optically inactive, or racemic.

**D-amino acids are encountered in some species of bacteria (see below), but not as constituents of protein.

subject of debate ever since Pasteur's pioneering studies of molecular asymmetry.

In 1848 Pasteur discovered the enantiomerism of sodium ammonium tartrate (37). A supersaturated solution of optically inactive sodium ammonium tartrate crystallised as large hemihedral crystals, some of which were visibly right-handed and some left-handed. Upon separation of the two forms with tweezers, Pasteur found that one form imparted a dextrorotatory turn to plane-polarised light and the other form a laevorotatory one. He subsequently established the asymmetry of other organic molecules (38). Pasteur held that asymmetric molecules could not be produced by purely chemical means, but required the action of an asymmetric force. His observation that yeast cells "select" the D-enantiomer from optically inactive mixtures of sugars suggested that vital activity constituted this asymmetric force (39). However, Pasteur did not exclude the possibility that some physical asymmetric force might lead to the production of asymmetric molecules and suggested that the magnetic field of the earth might prove to be such a force*. His own attempts to confirm this were unsuccessful but he continued to search for natural asymmetric principles of a cosmic order and saw the asymmetry of life as a function of the asymmetry of the universe (40).

On Pasteur's theory of molecular asymmetry, the optically inactive form of potentially asymmetric molecules which is produced in the absence of an asymmetric force was not simply a mixture of the two enantiomers but a single compound molecule, internally

*In fact, magnetic fields are not fundamentally asymmetric forces.

compensated for asymmetric effects. This theory was undermined by the concept of the asymmetric carbon atom, formulated independently by van 't Hoff and Le Bel in 1874 on the basis of Butlerov's idea of the tetrahedral arrangement of the tetravalent carbon atom (41). According to the new theory, there were only two molecular forms of each compound with one asymmetric atom and the optically inactive form was always an equal mixture of the two. In other words, asymmetric molecules are formed even in the absence of an asymmetric force but the two enantiomers are formed in equal numbers so that there is no net optical activity.

The theory of the asymmetric carbon atom could not, however, explain the selective production of optically active molecules by living organisms and the relation between molecular asymmetry and life remained problematic. In 1898 F.R. Japp argued for the inseparability of the questions of the origin of molecular asymmetry and of the origin of life (42). Starting with an asymmetric molecule, it was straightforward enough to synthesise other asymmetric molecules, but this did not explain the absolute origin of molecular asymmetry. According to Japp, the production of net molecular asymmetry was the prerogative of life, which implied that a directive force, irreducible to physics and chemistry, was at work in living organisms. Japp categorically denied the possibility that net asymmetric synthesis could take place outside living organisms and argued in favour of vitalism on this basis. His argument was criticised in a protracted correspondence in Nature, where his lecture had been published. Karl Pearson, for example, argued that even purely mechanical action would in the long term lead to the preponderance of one-sided asymmetry due to statistical deviations from the expected 1:1 distribution. Once one enantiomer was preponderant it would become a "breeder" for other asymmetric forms (43).

In the meantime, the search for a physical asymmetric force continued and circularly polarised light was proposed as a suitable candidate in the 1890s. In 1904, A. Byk argued that the selective synthesis of one particular enantiomer of organic molecules on earth might be accounted for by the fact that dextro-circularly polarised light predominates in reflected sunlight at the earth's surface (44). His own attempts to confirm this hypothesis were unsuccessful but in the 1930s several workers achieved the asymmetric synthesis of organic molecules using circularly polarised light (45). Since then, there have been many demonstrations of net asymmetric synthesis under the influence of asymmetric physical forces and spontaneously as a result of statistical events (46). Hence, there are factors in inorganic nature that might account for the selective formation of optically active molecules before the appearance of life on earth.

However, it is also known that the steric configuration of enzymes, for example, is crucial for their activity. Here the overall shape of the molecule is as important as its primary structure and this three-dimensional configuration would be lost if its monomeric subunits were not of a single chirality (47). The complex polymers encountered in living organisms, such as the proteins and nucleic acids, are usually regarded as the products of prolonged biological evolution and this raises the question of whether the molecular asymmetry of life is in fact a product of evolution, even if net asymmetry is not absolutely confined to the living world. In other words, were the first living systems asymmetric at the molecular level because of the preponderance of particular enantiomers in the prebiotic environment, or did the ability of organisms to select and incorporate molecules of uniform chirality from an essentially symmetric environment evolve gradually? Convincing arguments in favour of the latter position were presented by George Wald in 1957 (48). He pointed out that all inorganic sources of optical activity require very restricted conditions, produce poor net yields of stereospecificity and tend to result only in local and temporary asymmetry. For these reasons, he suggested that strict asymmetry arose as a consequence of intrinsic structural demands of the key molecules of which organisms eventually came to be composed, through the selection of particular enantiomers from racemic mixtures. Besides experimental evidence that the artificial substitution of D-amino acids for L-amino acids in polypeptide chains leads to a progressive decrease in the stability of the secondary structure of the polypeptides, there are theoretical arguments in favour of this view. For example, the presence of D-amino acids in certain bacteria suggests that the early ancestors of these organisms were less stereospecific than organisms higher on the phylogenetic scale. Moreover, the puzzling presence of the enzyme D-amino oxidase in mammalian liver could be interpreted as an evolutionary vestige of a mechanism that eliminates the "wrong" amino acids (49).

One of the consequences of this biogenic hypothesis of the origin of the molecular asymmetry of life is that the initial "preference" of organisms for one enantiomer rather than its mirror image can only be accounted for on the basis of chance. Perhaps it is this feature of the biogenic hypothesis which is less attractive to deterministically minded scientists, as it was to Oparin. Throughout his writings, Oparin favoured an abiogenic origin of the asymmetry of life while he opted for an evolutionary, biogenic, view in virtually all other instances of "chicken-and-egg" questions (such as the origin of the genetic code, the specificity of enzymes, etc.). It is not clear, however, whether Oparin regarded the high degree of stereospecificity that is encountered in modern organisms as a product of physical forces alone, or whether he thought that a slight net asymmetry in the prebiotic environment would necessarily have pushed a subsequent evolutionary development towards virtually absolute stereospecificity into the direction it has taken. The latter position would be consistent both with a deterministic view and with Oparin's general philosophy of the inseparability of the evolution of living organisms and of their fundamental characteristics.

Certain tests can be suggested: do mixed polymers of, say, L- and D-amino acids form stable coacervates? If not, then the stereospecificity of even precellular systems may have been very high, thus favouring an abiogenic view. But if they do, it would seem more likely that a secondary elimination of "mixed" systems resulted from the evolutionary development of coacervates containing more efficient polymers of a higher degree of stereospecificity. A test between the chance hypothesis and the deterministic version of the biogenic position outlined above may eventually be provided by space exploration. If life based on enantiomers of different chirality from those on earth is encountered on another planet where any physical asymmetric forces act in the same direction as on earth, then Wald's chance hypothesis would be favoured. A single instance of life, on such a planet, which exhibits the same chirality as on earth would, unfortunately, be inconclusive. In any case, demonstrations of asymmetric syntheses by abiogenic means cannot, on their own, settle the dispute.

The origin of the eukaryotic cell: A less fundamental, but equally problematic question concerns the origin of the eukaryotic cell, which is sharply distinguished from prokaryotes by its specialised internal organelles bound by membranes such as the nucleus, mitochondrion and chloroplast. Because the microfossil record suggests that eukaryotes were comparative late-comers in phylogenetic development, long after the origin of the earliest organisms, this question will be touched on only briefly here.

In 1905 Mereschkowsky suggested that the chloroplasts of plant cells were originally free-living Cyanophyceae (blue-green algae) which had developed a symbiotic existence with an amoeboid organism (50). In a later paper (51) Mereschkowsky developed his arguments in greater detail and listed a number of what he thought were fundamental differences between the "mycoplasma" of bacteria, fungi and algae and the "amoeboplasma" of plant and animal cells. These differences included oxygen requirement*, temperature resistance, metabolic requirements for organic substrates, mobility and chemical parameters such as phosphorus content. These differences suggested an independent origin of the two types of plasma to Mereschkowsky and he proposed that life had started independently with a "mycoid" biococcus and, later, at lower temperatures, an amoeboid Moneron without nucleus. The symbiosis of these two types led to the development of amoebae (with nucleus), some of which were subsequently invaded by haplobacteria (e.g. Cyanophyceae), which had descended directly from the biococcus, to give rise to plant and animal cells. This was the first, rather primitive, version of the "serial endosymbiotic theory" of the origin of the eukaryotic cell.

Today the concept of the symbiotic origin of the eukaryotic cell has a large following and the theory has been particularly well developed by Lynn Margulis (53). The comparative autonomy of mitochondria and chloroplasts received support from the discovery that these organelles contain DNA and mechanisms for the synthesis of certain proteins that are not coded for by the nuclear genome. Moreover, mitochondria are similar in size to bacteria, they contain phosphorylating respiratory chains with cytochromes in their membranes, as do aerobic bacteria, and they respond in similar ways to uncouplers and inhibitors of oxidative phosphorylation. Chloroplast rRNA hybridises with the DNA of blue-green algae, and chloroplast ferredoxins show marked similarities to the ferredoxin of the blue-green alga _Nostoc_ (54).

*Mereschkowsky, incidentally, observed that most bacteria are anaerobic and that aerobic bacteria are often capable of adapting to anaerobic conditions. He concluded that the earliest forms of life must have been anaerobic and probably originated when the earth's seas were still boiling and had no oxygen dissolved in them (52).

Many more data in support of an independent prokaryotic origin of mitochondria and chloroplasts could be cited, but here only general lines of argument will be discussed.

The opponents of the symbiotic theory believe that the eukaryotic cell is the result of a long process of evolution along a single path of development. This was the position adopted by Oparin, for example, who rejected the symbiotic theory on the grounds that it conflicts with evolutionary philosophy, according to which the evolution of complex structures is an integrated process (55). To Oparin, it would be as absurd to claim that a mitochondrion, say, could have evolved independently as it was for Empedocles to claim that arms, eyes and legs evolved first and then combined into a whole body. Others have pointed out that it is hard to understand how the hypothetical "proto-eukaryote" devoid of respiratory and photosynthetic equipment could have competed successfully with existing aerobic and photosynthetic prokaryotes before it acquired its endosymbionts (56). Such general objections as well as more detailed ones (for example a number based on sequencing studies of cytochromes) have led to the formulation of alternative hypotheses in which the mitochondrion is regarded as a "snipped off" portion of the invaginated membrane (with respiratory function) of an aerobic prokaryote. On this view, a stable plasmid containing mitochondrial genes was established before the respiratory organelle acquired an outer membrane (57).

Before this dispute can be settled, many experimental and theoretical advances are required. In particular, most of what is known about the molecular basis of gene function is derived from studies with viruses and bacteria. It is now clear that mechanisms of protein synthesis and their control are much more complex in eukaryotes, but the details are only just beginning to be worked out. Recent studies of the coding mechanism for protein synthesis directed by mitochondrial DNA have demonstrated a divergence from what was believed to be the universal genetic code*. Last year, Tzagoloff and his co-workers showed that in yeast mitochondrial DNA the UGA triplet, which elsewhere serves as a terminator, codes for tryptophan (59). Since then, other anomalies have been found (60). This result is particularly puzzling with respect to the origin of the eukaryotic cell in that the mitochondrial code departs both from that of bacteria and that of the eukaryotic nuclear genome. The mitochondrial code may have resulted from an evolutionary change or it may represent a code used by highly primitive organisms. However, its implications for hypotheses on the origin of the eukaryotic cell are not straightforward. In view of the uncertainty regarding the detailed mechanisms and the evolutionary significance of organellar protein synthesis, the transition from prokaryotes to eukaryotic cells is likely to remain problematic for some time to come.

All the questions outlined in this section have methodological implications. For example, a scientist living at the turn of

*Evidence has also been found recently which suggests that different taxonomic groups use the genetic code differently (58). Each group has a particular coding "strategy" in that it consistently selects one codon from synonymous ones, i.e. base triplets that code for the same amino acid.

the century who agreed with Japp would have found it futile to try and synthesise stereospecific enantiomers by physical means alone. Similarly, Oparin and his followers would not care to formulate hypotheses on the abiogenic development of translation mechanisms for protein synthesis, or search for an as yet undiscovered bacterium that may reveal close homology with mitochondria. In all cases, the problem concerns the explanation of transitions that must, at some stage, have occurred during chemical or biological evolution. What is the most fruitful approach to the questions of how and at what stage such transitions occurred?

Laws and matter: the problem of transitions

Biologists have repeatedly run into difficulties when they have made attempts to define life. Such definitions tend to be based on criteria that include objects that intuitively are not alive (such as inorganic crystals if growth is the main criterion) or exclude organisms that are (such as mules and worker bees if the capacity to reproduce is used as a criterion). This difficulty is circumvented to a large extent by an evolutionary theory of the origin of life. The decision to call any particular system along the general path of development alive then becomes largely arbitrary, but not trivial. Many years ago, Pirie compared the transition from the non-living to the living with that between, say, yellow and green (61). The transition is gradual, but a distinction between the two is still useful. In the case of colours, however, one single parameter (wavelength) is involved while no single property adequately distinguishes the living from the non-living. In the case of life, the origin of a whole series of features needs to be explained and decisions have to be made on the order in which each transition is likely to have taken place. Which properties arose abiogenically, which arose inside precellular open systems, and which arose only after primitive living organisms had come into being? In general, which features must have evolved before we can speak of living organisms, however primitive? There are no a priori rules that provide definite answers to these questions; the questions shift and provisional answers change by the continual interplay between theory and empirical observation*. Are there, however, any general methodological dictates or constraints that may serve as underlying guiding principles?

One general constraint, discussed in the context of theories of the origin of life by Peter Mora in 1963 (63), may be provided by the demand that we do not attempt to explain developmental processes at one level (e.g. the physical level) in terms of laws that only operate at higher levels of development (e.g. the biological level). Mora was particularly critical of the application of the concept of natural selection to preliving systems in theories such as that of Oparin. In particular, the concept of natural selection should not be used to explain the origin of the first self-reproducing systems,

*Oparin's writings provide a case in point. In his first paper Oparin saw the transition to life taking place with the formation of the first piece of colloidal gel (i.e. with the origin of individuality). In 1936, he insisted that coacervates capable of metabolism became alive only when they were subject to natural selection. In 1957 he wrote that natural selection only operated on systems capable of "purposive adaptation" and in 1966 he suggested that a high degree of internal coordination, with the aid of enzymes of high specificity, and molecular mechanisms of replication and protein synthesis were prerequisites for the operation of natural selection and, hence, for life (62).

nor should it be applied at the level of single molecules (64).

Oparin, of course, agreed that it was meaningless to talk of the natural selection of single molecules. Besides his opposition to the idea of the evolution of the hereditary material in the general environment (see Chapter X), he objected to Calvin's concept of the evolution of enzymes outside pre-vital and vital systems. What possible advantage could be conveyed to an enzyme that was slightly more efficient at catalysing, say, the decarboxylation of pyruvate? Surely, it was the system within which the enzyme operated that had selective advantage over others (65). With respect to Mora's general point, however, Oparin defended the concept of "prebiological natural selection". According to Oparin, the development of living systems and the development of new biological regularities, expressible in terms of biological laws, went hand in hand (66). There is, on this view, a hierarchy of laws in nature, operating at different levels of development. However, the transitions between these levels are gradual and Mora's concept of an impassable gap between physical and biological laws is rejected: incipient biological laws were at work in incipient living systems. In other words, while Oparin supported the idea that there are fundamental qualitative distinctions between different levels of development, he did not formulate his hypotheses in terms of dialectical "leaps".

Graham has stated in this context that there is a lack of precision in definition in Oparin's philosophy of biology (67). It is true that there is a lack of precision in the definition of transitions between different levels of development in Oparin's theory of the origin of life, but it is arguable to what extent this is the result of philosophical limitations or of gaps in empirical knowledge. Through the years, Oparin's theory gained in precision greatly with the acquisition of new scientific knowledge and there is no obvious reason why this process should not continue. Nevertheless, there are conceptual difficulties in many areas of science that are concerned with developmental transitions, for example in the study of cell differentiation and embryological development and of processes of ageing in organisms. Philosophers of science should aim to develop a consistent methodology for the historical and developmental sciences. Such a methodology should go beyond the generalities of the Hegelian dialectic and avoid the pitfalls of reducing the behaviour of complex systems to the properties of only one or two of its components.

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